Diagnosis and Management of Infectious Diseases

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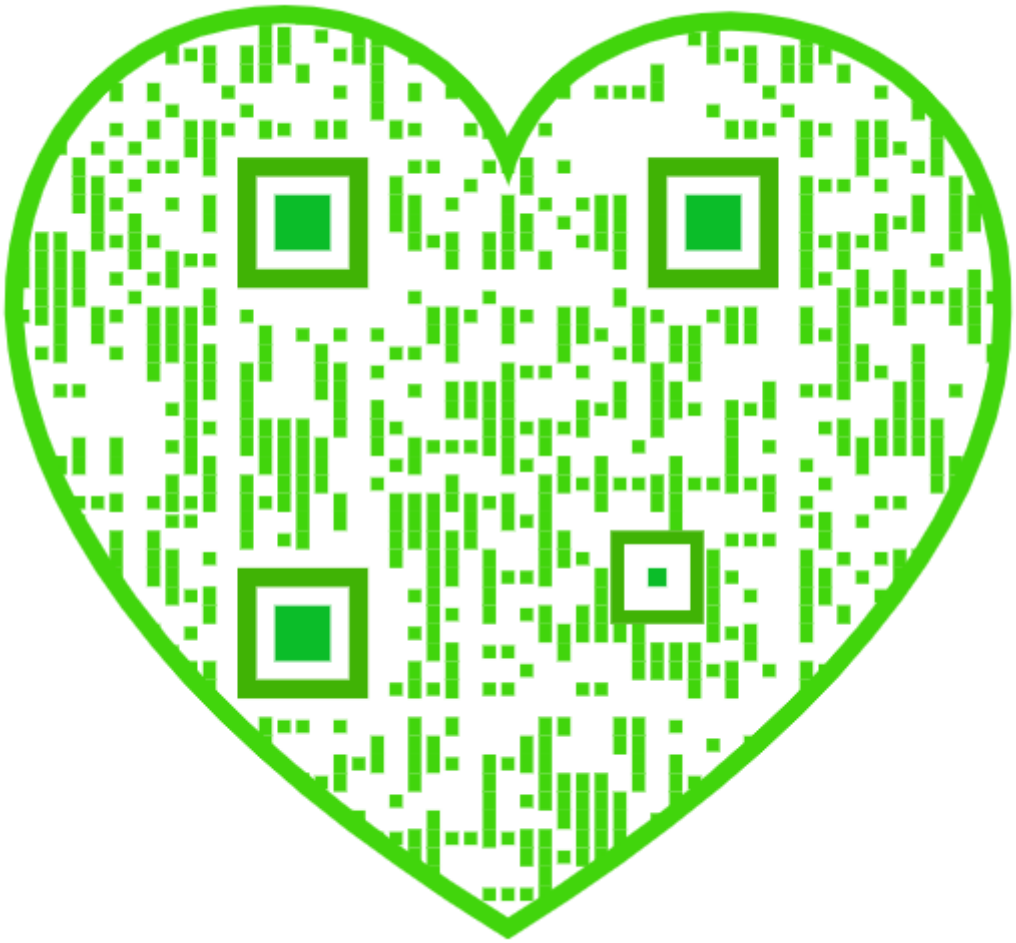

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PREFACE

This book arises from numerous requests from several classes of people over many years.

The original version was a short *Beginner's Guide* (subtitled *Everything You Always Wanted to Know about Microbiology but Were Too Dumb to Ask*) for branch managers and similar personnel required to assume a role in microbiology but with limited experience and training.

This has been gradually expanded and modified to suit the needs also of more experienced laboratory practitioners; researchers; medical, medical laboratory science and science students; and medical practitioners.

The work is in four parts. The first deals with clinical conditions, diseases and syndromes under the various organ systems. For each of these, causative agents, diagnosis, treatment and, where appropriate, prophylaxis, prevention and control are given, together with some general notes. Recommended treatments are current consensus opinions from a variety of authoritative sources but may not be the most suitable in all situations. Practitioners should always be guided by individual circumstances and local patterns and should always verify dosages and precautions from package inserts.

Part II presents, by taxonomic order, descriptions of all the medically important organisms, including taxonomy and identification, conditions caused, some details of pathogenesis and immune response, diagnosis and treatment.

Part III systematically presents descriptions of agents used in treatment, their basic characteristics, uses and side-effects and other relevant details.

Part IV constitutes an outline of important facets of laboratory practice.

References are not included, since these would have required a book as large as the existing work. I freely acknowledge my debt to the thousands of colleagues who have directly or indirectly contributed.

Part I: Clinical Conditions, Diseases and Syndromes

Chapter 1

Infections of the Respiratory Tract and Associated Structures

ANTIBIOTICS are commonly unnecessarily prescribed for respiratory infections entirely due to viral infection. Recent research indicates that procalcitonin levels of > 0.25 μg/L are associated with bacterial infections, while lower levels are unlikely to be found if bacterial infection is present.

COUGH is the presenting symptom in 6% of new episodes of illness in the UK and is responsible for 0.1% of ambulatory care visits in the USA. It is a common symptom of upper respiratory infections, occurring in 81% of patients with influenza A, in parainfluenza, rhinovirus infections and rotaviral respiratory tract infection. With influenza B, incidence of cough as a symptom varies with age: 99% in young adults, 86% in pre-school children, 61% in school-age children, and 60% in older adults. Infections with adenovirus 3, 4, 7, 14 and 16 are associated with cough in only about 7% of patients, and echovirus 9 in 15%. Cough is, of course, a prominent and invariant feature of whooping cough. Productive cough is common in pneumonia, but shows variability with agent: 73% with *Mycoplasma*, 69% in pneumococcal, 47% in psittacosis, 44% in legionellosis (persisting several weeks). Respiratory syncytial virus infections are associated with cough in 80% of patients with pneumonia and 63% of bronchiolitis cases. Cough in tuberculosis is usually productive and persisting for several weeks. Paragonimiasis is associated with the production of tenacious brown or red sputum in 30% of cases. Cough also occurs in a number of intestinal infections: 39% of cases of typhoid fever, 25% of travellers' diarrhoea, 19% of cholera, 17% of *Escherichia coli* infections, 13% of salmonellosis, 12% of *Shigella* infections and 8% of *Aeromonas hydrophila* infections. A dry cough is noted in 41% of cases of acute schistosomiasis, while ascariasis is also associated with cough. Systemic viral infections associated with cough include atypical measles, measles and rubella. Cough may also be due to chemical exposure or associated with protein energy malnutrition.

Treatment:

Mild Cases (Respiratory Rate < 50-70/min): honey; 'cough potion' (spearmint + amaranth +ammonium chloride) + paracetamol if axillary temperature > 39°C + salbutamol if > 1 y and wheezing

Moderate Cases (Respiratory Rate 50-70/min): as above + penicillin (50,000 U/kg/d i.m.) or cotrimoxazole

Severe Cases (Respiratory Rate > 70/min): single dose of antibiotic and hospital admission

ACUTE RESPIRATORY ILLNESS: Acute respiratory disease due to a variety of viral agents is probably the commonest human disease.

Agents: adenovirus, parainfluenza, influenza, echovirus, reovirus, coxsackie A21, B1-5, respiratory syncytial virus, *Mycoplasma pneumoniae, Coxiella burnetii,* etc

Diagnosis: EIA (sensitivity 90%) or DFA (sensitivity 80%) and viral culture (shell vial assay sensitivity 95%, extended culture sensitivity 54%) of nasopharyngeal aspirate or cytobrush nasopharyngeal swab (sensitivity ≈ 70% for nasopharyngeal aspirate); serology

Treatment:

Viruses: non-specific

M.pneumoniae, C.burnetii: tetracycline

UPPER RESPIRATORY TRACT INFECTION, COMMON COLD, FEVERISH COLD: commonest contagious disease; 31% of acute illness in the USA and 5% of new episodes of illness in the UK; causes 12% of fever in returned travellers to Australia; transmission by airborne droplets and by touching contaminated objects; incubation period 1-4 d

Agents: rhinovirus (bronchitis-like cold; incubation period 2 d; duration of illness 10 d; cough in 60%, malaise in 25%, fever in 15%), coronavirus (incubation period 3 d; duration of illness 7 d; malaise in 45%, cough in 35%, fever in 20%), influenza A (usually with fever; winter), B (usually with fever; winter), C, parainfluenza (in 30% of infections), echovirus 4, 7 (in 14% of infections), 8, 11 (in 9% of infections), 19, 20, 22, 25, 30, respiratory syncytial virus (bronchitis-like cold; in 80% of pneumonia and 53% of bronchiolitis cases due to this agent),

Rotavirus (in 33% of infections in patients < 6 mo and 19% > 6 mo), adenovirus (bronchitis-like cold), coxsackievirus A10, 21, 24, B3-5, human metapneumovirus (15% of cases in children; mild to severe); also *Mycoplasma pneumoniae* (atypical pneumonia-like disease)

Diagnosis: mild to moderate dry cough and chest discomfort, mild malaise, stuffy nose, sneezing, sore throat; viral culture of nasal swab, throat swab, sputum, faeces; immunofluorescence of pharyngeal aspirate; ELISA (antigen) on nasopharyngeal secretions; complement fixation, haemagglutination inhibition, neutralisation; PCR

Respiratory Syncytial Virus: acute wheezing common; lymphocytosis with neutropenia, becoming neutrophilia if secondary bacterial infection

Treatment: paracetamol, hydration, oral (not < 12 y, diabetes, heart disease, hypertension, prostatic hypertrophy, hyperthyroidism) or topical decongestant (not < 6 mo) for not more than 5 d, antihistamines, steam inhalations, nasal saline irrigation, ipratropium bromide 21 µg/spray 4 sprays into each nostril or 42 µg/spray 2 sprays into each nostril to 3-4 times daily reducing as rhinorrhoea improves for up to 4 d

Prophylaxis: α_2-interferon spray 5 MU daily for 7 d; experimental vaccines and antiviral drugs

Upper Respiratory Tract Infection Symptoms also occur in 62% of cases of travellers' diarrhoea, in *Norovirus* infections and poliomyelitis and in < 10% of *Haemophilus influenzae* conjunctivitis.

Coryza: watery discharge from nose, becoming purulent; no systemic symptoms; course 7-10 d; RSV infection in 30% of cases; common with influenza A, influenza B (in 91% of infected young adults, 72% of infected pre-school children and 66% of infected school-age children), influenza C, parainfluenza, measles, rubella and infections with adenovirus 3, 4, 7, 14, *Mycoplasma hominis*; occurs also in a few patients with intestinal infections: 10% of *Shigella* infections, 8% of *Salmonella*, 6% of *Aeromonas hydrophila* and 4% of cholera and enterotoxigenic *Escherichia coli* infections

Rhinitis

Agents: coronavirus, rhinovirus, influenza, parainfluenza, respiratory syncytial virus, enteroviruses, adenovirus, reovirus; also 10-25% of cases of infectious mononucleosis and in primary amoebic meningoencephalitis

Diagnosis: viral culture of nasal swab, washings; serology; exclude CSF leak

Treatment: paracetamol, hydration, oral (not < 12 y, diabetes, heart disease, hypertension, prostatic hypertrophy, hyperthyroidism) or topical decongestant (not < 6 mo) for not more than 5 d, antihistamines, steam inhalations, nasal saline irrigation, ipratropium bromide 21 µg/spray 4 sprays into each nostril or 42 µg/spray 2 sprays into each nostril to 3-4 times daily reducing as rhinorrhoea improves for up to 4 d

Rhinosporidiosis

Agent: *Rhinosporidum seberi*

Diagnosis: microscopy of infected material from nose, pharynx, larynx, eye, lacrimal sac, skin; histology of polyps

Treatment: natamycin

Nasopharyngitis: 4% of new episodes of illness in the UK

Agents: parainfluenza 1, 2, *Haemophilus influenzae, Streptococcus pyogenes, Streptococcus pneumoniae*

Diagnosis: culture of nasopharyngeal swab, nasal swab, throat swab

Treatment: amoxycillin, cefuroxime axetil, cefpodoxime, erythromycin

Resistant *Streptococcus pneumoniae:* clindamycin, grepafloxacin, levofloxacin, sparfloxacin, trovafloxacin

Rhinoscleroma (Scleroma Nasi): a granulomatous disease of the nasopharynx characterised by the formation of hard, crusted, patchy or nodular lesions; endemic in northern and central Africa, S E Asia, Central America

Agent: believed to be caused by *Klebsiella pneumonia subsp rhinoscleromatis*

Diagnosis: clinical; culture of pus from sinus

Treatment: cotrimoxazole for 1 mo to several mo; surgery where indicated

Oronasopharyngeal Histoplasmosis

Agent: *Histoplasma capsulatum*

Diagnosis: intracellular, oval yeast cells in mononuclears on biopsy; fungal culture of biopsy or swab at 25°C and 35°C; hypochromic anemia and leucopenia; in children, lymphocytosis with atypical mononuclears

Treatment: amphotericin B, ketoconazole

NASOPHARYNGEAL AND ORONASAL LEISHMANIASIS
Agents: *Leishmania braziliensis* (espundia; severe form of leishmaniasis that may occur months or years after the cutaneous form of the disease, characterised by erosive lesions that may cause extensive destruction of nasopharyngeal tissues; usually fatal if untreated), *Leishmania mexicana* (rare; lesions on mucous membranes)
Diagnosis: examination of smears of tissue or aspirate from lesion; culture of tissue or exudate; IFA, ELISA
Treatment: sodium stibogluconate
NASOPHARYNGEAL MYIASIS: infestation of nares and/or pharynx by larvae of certain flies
Agents: *Chrysomya bezziana*, *Chrysomya megacephala, Cochliomyia hominivorax, Cochliomyia macellaria, Oestrus ovis, Lucilia sericata, Rhinoestrus purpureus, Wohlfahrtia vigil*
Diagnosis: pain, purulent nasal discharge, nasal obstruction; may be extensive tissue destruction; sometimes fatal
Treatment: removal
HALZOUN (MARRARA): acute oedematous condition of upper respiratory tract
Agents: usually *Linguatula serrata* (nasopharyngeal); also *Fasciola hepatica* (pharynx) and *Limnatis nilotica* (larynx or trachea)
Diagnosis: direct visualisation
Treatment: levamisole
LAGOCHILASCARIASIS: infestation of tonsils and nose; occasional metastatic abscesses; Brazil, Colombia, Costa Rica, Mexico, Tobago, Trinidad, Venezuela
Agent: *Lagochilascaris minor*
Diagnosis: usually detected by migration of worms through mouth or nose or by visualisation during tonsillectomy
Treatment: levamisole 150 mg orally 8 hourly for 8 d, then 150 mg orally 12 hourly for 3 days of the week for 12 w (child: 150 mg orally 8 hourly for 15 d)
CATARRH
Agents: measles, rubella, other viruses, *Bordetella pertussis*
Diagnosis: viral culture of throat swab, bacterial culture of nasopharyngeal swab plated directly to charcoal agar; serology
Treatment: hydration, steam
Bordetella pertussis: erythromycin
ACUTE SINUSITIS: symptoms < 4 w; mainly maxillary; 0.5% of new episodes of illness in UK; 0.2% of ambulatory care visits in USA; viral sinusitis in 39%, and bacterial sinusitis in 0.5-2.5%, of patients (5-15% of children) with common cold
Agents: 20-36% *Streptococcus pneumoniae,* 15-30% *Haemophilus influenzae* (nontypeable strains; 13% of sphenoid), 9-15% rhinovirus, 9% α-streptococci, 7-19% *Moraxella catarrhalis*, 5-10% anaerobes, 3% *Streptococcus viridans*, 3% β-haemolytic streptococci not group A (including *Streptococcus milleri*, group C also frontal), 2-9% Gram negative enteric bacteria, 2-5% influenza virus, 2-3% *Streptococcus pyogenes*, 1-6% *Staphylococcus aureus* (56% of sphenoid), 1% *Pseudomonas aeruginosa* (increased in AIDS), 1% parainfluenza 2, 1% parainfluenza 3; adenovirus (2% in children), *Legionella pneumophila* (in AIDS), measles (in 2% of cases), *Capnocytophaga*, *Salmonella* (in renal transplant recipients), *Chlamydophila pneumoniae*, *Moraxella lacunata, Pasteurella multocida, Haemophilus aprophilus*, *Haemophilus paraprophilus*; no growth in 20-25% of cases; may be initial manifestation of *Acanthamoeba* infection in AIDS
Diagnosis (Bacterial): persistent mucopurulent nasal discharge (> 7 d), postnasal drainaage, anosmia, nasal congestion, prolonged fever, facial pain, headache, cough, tenderness over sinuses (especially unilateral maxillary tenderness), tenderness on percussion of maxillary molar or premolar teeth that cannot be attributed to a single tooth, headache, daark circles under eyes, periorbital edema, lymphoid hyperplasia, purulent material in pharynx, poor response to decongestants; in children, also irritability, vomiting, gagging on mucus, prolonged cough; culture of maxillary sinus aspirate; serology; microimmunofluorescent antibody to *Chlamydophila pneumoniae* (IgG and IgM in paired sera 6-8 w apart)
Differential Diagnosis: dental neuralgia (careful dental examination), temperomandibular neuralgia (location of pain, careful history and observation), trigeminal neuralgia (pain over fifth cranial nerve distribution only), migraine (history of similar pain on previous occasions), temporal arteritis (location of pain and tenderness), erysipelas (swelling and stippling of skin surface), nasal diphtheria (extremely rare), typhoid fever (extremely rare)

Treatment: oxymetazoline, tramazoline or xylometazoline 2-3 drops into each nostril 2-3 times daily for 5 d; pseudoephedrine; paracetamol ± codeine

Pseudomonas aeruginosa: ticarcillin + gentamicin ± surgical drainage

Legionella pneumophila: erythromycin, fluoroquinolone

Other Bacteria: amoxycillin 15 mg/kg to 500 mg orally 8 hourly for 5-7 d

Amoxycillin Resistant or Unresponsive: amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 8 hourly

Penicillin Hypersensitive: cefuroxime 10 mg/kg to 500 mg orally 12 hourly for 5-7 d, cefaclor 375 mg orally 12 hourly (child: 10 mg/kg to 250 mg orally 8 hourly) for 5-7 d, doxycycline (not < 8 y) 2.5 mg/kg to 100 mg orally daily for 5-7 d, levofloxacin 500 mg daily

CHRONIC SINUSITIS: symptoms persist > 8 w; 1.7% of ambulatory care visits in USA

Agents: 31% *Prevotells* (71% of sphenoid), 22% anaerobic streptococci (57% of sphenoid), 21% other streptococci, 16% *Fusobacterium* (57% of sphenoid), 16% *Pseudomonas aeruginosa,* 16% *Haemophilus influenzae*, 10% *Staphylococcus aureus,* 10% *Moraxella catarrhalis*; various fungi (acute (fulminant), chronic (indolent) invasive, fungus ball, allergic fungal sinusitis; 25% *Aspergillus* (*A.flavus*—frequently pansinusitis, especially in cancer patients—*A.fumigatus, A.niger, A.oryzae*), 23% *Curvularia*, 16% *Bipolaris* (predominant agent in allergic fungal sinusitis), 12% *Fusarium,* 9% *Penicillium*, 8% *Alternaria*, 4% *Cladosporium*, 1% *Drechslera*, 1% *Exserohilum*, 1% *Mortierella hyaline;* also *Acremonium, Chaetoconidium, Coniothyrium, Chrysosporium, Geotrichum, Paecilomyces, Scedosporium prolificans, Schizophyllum*, *Pseudallescheria boydii* in immunocompromised); *Klebsiella pneumoniae* 14% of sphenoid, *Escherichia coli* 14% of sphenoid, *Pseudomonas aeruginosa* 14% of sphenoid; 25-60% no growth

Diagnosis: computed tomography, nasal cytology, nasal-sinus biopsy, tests for immunodeficiency, cystic fibrosis, ciliary dysfunction

Bacterial: culture of antral washings

Fungal:

Acute: 70% in diabetics; also in chronic renal failure or diarrhoea, immunosuppressive states secondary to chemotherapy, hematological disorders, transplantation, AIDS; cranial nerve deficit, proptosis, facial swelling, palatal ulcer, coma, stupor; pale to red to black necrotic areas involving turbinates or septum; microscopy, culture and histology of biopsy; radiographic evaluation with CT and MRI

Chronic Invasive: immunocompetent and atopic hosts; microscopy, culture and histology of biopsy

Fungus Ball: no symptoms, rhinorrhoea, nasal obstruction, facial fullness; X-rays or CT scan, microscopy and culture

Allergic: nasal obstruction, polyposis, history of multiple sinus procedures; polyposis, allergic mucin and thick, tenacious debris on nasal endoscopy; type I hypersensitivity confirmed by history, skin testing or serology; characteristic CT scan (complete unilateral or bilateral opacification of multiple paranasal sinuses; sinus expansion and erosion of a wall of involved sinus; scattered areas of intrasinus high attenuation amid mucosal thickening on noncontrasted CT); histologic evidence of eosinophilic mucus without evidence of fungal invasion into sinus tissue; positive fungal stain or culture of sinus contents removed intraoperatively or during endoscopy

Treatment: rule out allergy and structural abnormalities

Bacterial: surgical debridement; antibiotics as for acute infections; nebulised culture-specific antibiotics

Fungal:

Acute and Chronic Invasive: radical debridement + amphotericin B (***Pseudallescheria boydii****:* azole); intranasal amphotericin B 20 ml of 100 mg/L solution twice daily

Fungus Ball: complete removal via curettage with adequate ventilation

Allergic: surgery + oral prednisone + topical nasal steroids + nasal irrigations; fungal directed immunotherapy

Prophylaxis (*Aspergillus* Rhinosinusitis in Neutropenics): amphotericin B nasal spray, oral fluconazole

SORE THROAT: 6% of patients in general practice; 46% tonsillar adenitis, 15% pharyngitis, 14% tonsillitis, 3% acute laryngitis, 3% globus hystericus, 2% stomatitis (1% due to drugs), 1% chronic laryngitis, 1% quinsy, 1% myasthenia of larynx, 0.5% dysphagia, 0.5% infected tonsillar remnant, 0.5% postcricoid carcinoma, 0.5% aphthous ulcer, 0.5% submandibular calculus

Agents: see categories below; sore throat is also a symptom in 67% of cases of mycobacterial thyroiditis and 69% of thyroiditis due to other bacteria, in 36% of *Shigella* infections, 33% of Rocky Mountain spotted fever, 25% of cases of traveller's diarrhoea, 22% of cases of salmonellosis, 22% of Korean hemorrhagic fever cases, 12% of *Aeromonas hydrophila* infections, 10% of Norwalk gastroenteritis cases, 8% of enterotoxigenic *Escherichia coli* infections, 4% of cholera cases, and in cases of Lassa fever, reovirus infections, acute infectious nonbacterial gastroenteritis, aseptic meningitis, dengue, Ebola haemorrhagic fever, Marburg virus disease, measles, St Louis encephalitis, botulism, syphilis, toxic shock syndrome and toxoplasmosis

Diagnosis: clinical; see categories below

Treatment: see categories below

Aboriginals: single dose benzathine penicillin

Acute Throat Infections (Pharyngitis and Tonsillitis): incidence 30-40/1000; mainly in children and young adults; 3% of new episodes of illness in UK (streptococcal 0.04%); 1.7% of ambulatory care visits in USA (streptococcal 0.3%)

Agents:

Acute Exudative Tonsillitis: 35% no pathogen found; 23% viruses other than adenovirus (50% of echovirus 9 infections, 10% with exudate; 72% of influenza A cases; 25% of parainfluenza cases; in 60% of cases of pneumonia and 32% of cases of bronchiolitis due to respiratory syncytial virus; *human herpesvirus* 1; *Epstein-Barr virus* (in 66-85% of cases of infectious mononucleosis), 19% adenovirus (types 1-4, 5, 7, 14, 16; white spots may be present), 19% β-haemolytic streptococci other than *Streptococcus pyogenes* (mainly 'large colony' group C; groups B and G cause mild and self-limiting infections), 14% more than 1 agent, 12% *Streptococcus pyogenes* (streptococcal pharyngitis, septic angina, septic sore throat, streptococcal angina, streptococcal sore throat; infection is of pharynx, nasopharynx, nasal cavities and paranasal sinuses, not tonsils, at least in earlier stages), 5% *Mycoplasma pneumoniae*

Non-exudative Pharyngitis and Tonsillitis: enteroviruses, influenza B (in 100% of infected young adults, 78% of infected school-age children, 59% of infected pre-school children, 28% of infected older adults), rhinovirus, coxsackievirus (A1-6, 8-10, 16, 21, B2, 3, 5; herpangia; febrile in children), *Streptococcus pyogenes, Neisseria gonorrhoeae* (frequently asymptomatic but may be associated with inflammation and discharge), *Corynebacterium ulcerans, Arcanobacterium haemolyticum* (often with rash), *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae,* diphtheria (uncommon in Australia; causes fever ± exudate ± pseudomembrane), mixed anaerobes (necrotising ulcerative pharyngitis, fusospirochaetal angina, fusospirochaetal pharyngitis, Plaut angina, pseudomembranous angina, ulceromembranous angina, ulceromembranous pharyngitis, Vincent's angina), *Haemophilus influenzae, Actinomyces pyogenes, Candida albicans; Capnocytophaga* and *Fusobacterium* in neutropenics; 1 case due to *Cryptococcus neoformans* in patient with leukemia; agranulocytosis, leukemia and a variety of irritant chemical and physical agents may also mimic acute throat infection

Diagnosis: sore throat with pain on swallowing, fever, headache; *Streptococcus pyogenes* more likely in children 4-15 y and in febrile patients with exudative tonsillitis and cervical lymphadenopathy; herpangia and exanthem in coxsackievirus, echovirus 16, 17; many rapid commercial test kits for *Streptococcus pyogenes* (throat swab) sensitivity 76-95%, specificity 93-97%; Gram stain and Albert or Neisser stain, bacterial and viral culture of throat and tonsils; viral and mycoplasmal serology; microimmunofluorescent antibody or PCR-EIA for *Chlamydophila pneumoniae*; differential white cell count; blood cultures and excisional biopsy in neutropenics

Treatment: paracetamol, aspirin (adults) or ibuprofen; dexamethasone 10 mg single oral or i.m. dose; oral hydration; empirical treatment for streptococci is indicated for follicular tonsillitis with fever and local lymphadenitis, existing rheumatic heart disease, *Streptococcus pyogenes* prevalent in family or community, scarlet fever, quinsy

Streptococci: phenoxymethylpenicillin 10 mg/kg to 500 mg orally 12 hourly for 10 d; ampicillin, amoxycillin or amoxycillin-clavulanate should not be used as they are not superior to penicillin and are more likely to produce a rash, especially with *Lymphocryptovirus* infection, but also with other viruses

Remote Areas, Poorly Compliant, Intolerant of Oral Therapy: benzathine penicillin (3-6 kg: 225 mg; 6-10 kg: 337.5 mg; 10-15 kg: 450 mg; 15-20 kg: 675 mg; > 20 kg: 900 mg) i.m single dose

Penicillin Hypersensitive: roxithromycin 300 mg orally daily (child: 4 mg/kg to 150 mg orally 12 hourly) for 10 d

Recurrent or Treatment Failure: clindamycin 150 mg orally 6 hourly (child > 8y: 8-16 mg/kg daily in 3-4 divided doses) for 9 d, or amoxycillin-clavulanate

Neisseria gonorrhoeae: ceftriaxone 250 mg i.m. in lignocaine hydrochloride 1% as single dose or ciprofloxacin 500 mg orally in a single dose (not children or pregnant) + (if chlamydial infection is not ruled out) azithromycin 1 g orally in single dose or doxycycline 100 mg orally twice daily for 7 d (not < 8 y or pregnant)

Anaerobes: penicillin + metronidazole

Corynebacterium, Arcanobacterium haemolyticum: erythromycin 250 mg 4 times daily for 10 d

Mycoplasma pneumoniae, Chlamydophila pneumoniae: doxycycline 100 mg twice daily for 10 d, roxithromycin

Human herpesvirus: famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

Cryptococcus neoformans:

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

Other Viruses and Other Agents: saline gargles

PERITONSILLAR ABSCESS (QUINSY)

Agents: 30% *Peptostreptococcus,* 28% *Streptococcus pyogenes,* 16% *Peptococcus,* 9% *Fusobacterium,* 5% *Streptococcus pneumoniae,* 5% microaerophilic streptococci, 2% *Bacteroides fragilis,* 2% *Haemophilus influenzae,* 2% *Propionibacterium*, also *Corynebacterium ulcerans*, *Actinomyces pyogenes*

Diagnosis: Uni-Gold Streptococcal A Test and culture of deep swab of abscess

Treatment: surgical drainage or aspiration; benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly + metronidazole 12.5 mg/kg to 500 mg i.v. or 10 mg/kg to 400 mg orally 12 hourly till significant improvement then amoxycillin + clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 12 hourly; clindamycin 10 mg/kg to 450 mg i.v. or orally 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly till significant improvement then clindamycin 10 mg/kg to 450 mg orally 8 hourly

SCARLET FEVER (CANKER RASH, FEBRIS RUBRA, FEBRIS SCARLATINAE, FOTHERGILL DISEASE, SCARLATINA, SCARLATINA ANGINOSA): affects mainly children 6 mo to 3 y; latent period 1-2 d, incubation period 2-3 d, infectious period 14-21 d, interepidemic period 3-6 y

Agent: *Streptococcus pyogenes* producing erythrogenic toxin

Diagnosis: acute streptococcal infection (pharyngitis, wound infection, burn infection, puerperal fever) associated with skin rash (characteristically, punctate and erythematous) and 'strawberry' or 'raspberry' tongue ± conjunctivitis, rhinitis; desquamation of skin usually occurs; may be other toxic manifestations, including liver involvement; arthritis may occur; severity varies widely but, in general, disease is mild today; culture of nasal swab, throat swab; blood cultures; moderate neutrophilia

Treatment: penicillin, erythromycin, clindamycin

DIPHTHERIA (DIPHTERITIS): acute infectious disease involving the upper respiratory tract and, sometimes, skin; clinical manifestations primarily those of exotoxin; endemic and epidemic, world-wide; last reported case in Australia in 1993; tonsillar diphtheria (most common form, in which membrane is confined mainly to tonsils), pharyngeal (Bretonneau angina, Bretonneau diphtheria, Bretonneau disease, diphtheria cyanache, faucial diphtheria, malignant angina; uncommon form, occurring especially in persons without tonsils, in which membrane extends beyond faucial pillars; generally more severe than tonsillar form); 8% larynx (diphtheric laryngitis, garrotilla morbus suffocans; form that begins either in larynx—with frequent involvement of tonsils, nasopharynx or nose—or in trachea or bronchi; most common in children 2-5 y; relatively high rate of suffocation), nasal (membranous rhinitis; uncommon; relatively mild; membrane limited to mucosa of anterior nares) and nasopharyngeal (severe form with membrane formation on nasal, tonsillar and pharyngeal tissues), pharyngotracheobronchial diphtheria and tracheobronchial diphtheria, in which membrane extends into

tracheobronchial airways, causing increased risk of suffocation; myocarditis in 10% of cases, mortality 50%; bronchopneumonia in 8%, mortality 70%; bulbar paralysis in 4%, mortality 20%; peripheral nerve palsies in 2%, mortality 15%; latent period 2-5 d, incubation period 2-5 d, infectious period 14-21 d, interepidemic period 4-6 years

Agent: *Corynebacterium diphtheriae*

Diagnosis: sore throat, fever, malaise, headache, chills; death may result from either myocarditis or asphyxia

Tonsillar Diphtheria: pseudomembranous tonsillitis, cervical lymphadenopathy and a nasal watery discharge; occasionally complicated by otitis media or peritonsillar abscess

Severe Pharyngeal Diphtheria (Malignant Diphtheria, Diphtheria Gravis) and Nasopharyngeal Diphtheria: marked toxemia and massive swelling of neck ('bullneck'), sometimes followed by endocarditis

Albert's or Neisser stain, culture of blood agar, Tinsdale agar and Loeffler's medium of throat membrane fragments or throat swab in which membranous structure is sampled, and nasal swab; isolates of *Corynebacterium diphtheriae* and *Corynebacterium ulcerans* should be tested for toxin production

Treatment: antitoxin (500-1000 U/kg in nasal or mild pharyngeal, 1500 U/kg in moderately severe pharyngeal, 2000 U/kg in severe pharyngeal, 2500 U/kg in laryngobronchial) (always preceded by tests for allergy to horse serum and desensitisation if necessary) + procaine benzylpenicillin 1.2 MU/d (child: 25 000-50 000 U/kg/d) or parenteral erythromycin 40-50 mg/kg/d to maximum 2 g/d until patient can swallow comfortably, then oral erythromycin or phenoxymethylpenicillin 125-250 mg 4 times daily for total 14 d; endotracheal intubation for maintenance of airways; steroids for impending airways obstruction

Carriers: erythromycin 500 mg orally 6 hourly (child: 30-40 mg/kg daily in 3 divided doses) for 7 d, procaine penicillin 600 000 U (child: 12 500-25 000 U/kg) i.m. 12 hourly for 10 days + surveillance

Prophylaxis: highly effective live vaccine; hyperimmune immunoglobulin; isolation of cases until negative cultures of 2 samples at least 24 h apart after completion of antimicrobial therapy

Close Contacts: benzylpenicillin (< 6 y: 600 000 U; > 6 y: 1.2 MU) i.m. single dose or erythromycin (child: 40 mg/kg/d; adult: 1 g/d) for 7-10 d

OROPHARYNGEAL CANDIDIASIS

Agent: *Candida albicans*

Diagnosis: swab culture

Treatment:

Mild: miconazole 2% gel 50 mg (child < 1 y: 25 mg) orally 6 hourly for 1-2 w; amphotericin B 10 mg lozenge or 100 mg/mL suspension 1 mL orally 6 hourly for 1-2 w; nystatin 1 lozenge 100 000 U dissolved slowly in mouth 6 hourly for 7-14 d, or 1 mL 100 000 U/mL suspension orally 6 hourly for 7-14 d if lozenge not tolerated, clotrimazole 10 mg troche 5 times daily; gentian violet paint; cleaning of dentures and correction of poor fits if present

Severe (Immunocompromised including AIDS): fluconazole 3 mg/kg to 50 mg orally daily for 10-14 d or itraconazole 100 mg (10 mL) oral suspension daily for 10-14 d or miconazole 2% gel 2.5 mL orally 6 hourly for 10-14 d or nystatin liquid 100 000 U/mL 1 mL orally 6 hourly for 10-14 d, then fluconazole 50 mg orally daily or 150 mg weekly if frequent recurrences

Failure of Response: Does patient have diabetes mellitus? Is patient receiving oral antibiotics? Would eradication of gastrointestinal reservoir help? Is there a defect in immunity or any history of treatment with immunosuppressive drugs?

Prophylaxis (Immunosuppressed Patients): clotrimazole 10 mg 8 hourly as a lozenge; fluconazole 400 mg orally or i.v. daily

PHARYNGOCONJUNCTIVAL FEVER: occurs in children; associated with swimming pools

Agent: adenovirus 3, 4, 7, 14

Diagnosis: fever, sore throat, upper respiratory tract symptoms, conjunctivitis; viral culture of nasopharyngeal swab, conjunctival swab or scraping, faeces; serology

Treatment: non-specific

ACUTE LARYNGITIS: 0.8% of new episodes of illness in UK

Agents: parainfluenza 1 and 3, respiratory syncytial virus, adenovirus, influenza B, 4% of hospitalised measles cases

Diagnosis: hoarseness, barking or brassy cough without stidor in absence of lower respiratory tract signs; serology

Treatment: non-specific

ACUTE LARYNGEAL DYSPNEA: includes croup (acute laryngotracheobronchitis), acute epiglottitis and supraglottitis, laryngeal diphtheria; may also be due to angioneurotic oedema, foreign body or other laryngeal irritant, acute retropharyngeal abscess, papillomata of larynx, large infected prolapsing tonsils, peritonsillar abscess

Agents:

Croup: 80% viral (parainfluenza 1, 2, 3, influenza A (11% of total cases) and B, respiratory syncytial virus, adenovirus, enteroviruses, rhinovirus, measles virus, human metapneumovirus), 20% bacterial (*Streptococcus pneumoniae*, other streptococci, *Staphylococcus aureus, Corynebacterium diphtheriae*)

Acute Epiglottitis: *Haemophilus influenzae* (usually type b; also acute obstructive laryngotracheal infection), *Haemophilus parainfluenzae, Haemophilus paraprophilus, Streptococcus pneumoniae* (10% of adult cases), *Streptococcus pyogenes,* group C *Streptococcus* (single case)

Supraglottitis: *Haemophilus influenzae, Neisseria meningitidis* (0.3% of meningococcal infections)

Diphtheria: *Corynebacterium diphtheriae*

Diagnosis:

Croup: coryzal prodrome, hoarseness or husky voice, barking or brassy cough, inspiratory stridor ± sonorous rhonchi and coarse crepitation, variable airway obstruction; viral culture of nasal washings

Acute Epiglottitis and Supraglottitis are life-threatening situations which will usually be diagnosed clinically; typically children 2-7 y and adults; fever, sore throat, shortness of breath, rapid onset of dysphagia, pooling of secretions and drooling, sudden deterioration and death due to airway obstruction; note that fatal reactions have occurred on attempting to take swabs or even on examination of the oropharynx in acute epiglottitis; also that isolation of *Haemophilus influenzae* from throat swabs rarely implies acute epiglottitis; counterimmunoelectrophoresis or latex agglutination of serum may provide a diagnosis, while blood cultures are positive in 79-90% of cases

immunofluoresecence of pharyngeal aspirate or nasopharyngeal swab; Gram stain and Albert's or Neisser stain, bacterial and viral culture of laryngeal swab, nasal washings, nasopharyngeal aspirate; serology

Treatment:

Croup: usually self-limiting, lasting 2-7 d

Moderate to Severe: dexamethasone 0.3 mg/kg orally, prednis(ol)one 1 mg/kg orally, budesonide 2 mg by nebuliser

Significant Airway Obstruction or Fatigue: hospitalisation; dexamethasone 0.6 mg/kg orally or i.m. or prednis(ol)one 1 mg/kg orally + nebulised adrenaline 0.05 mL/kg/dose to 0.5 mL of 10 mg/mL solution diluted up to 3 mL with sodium chloride 0.9% solution or 0.5 mL/kg/dose to 5 mL of 1 mg/mL solution ± nebulised budesonide 2 mg/4 mL; tracheostomy or intubation if needed

Bacterial: erythromycin or penicillin + streptomycin

Epiglottitis and Supraglottitis: hospitalisation; intermittent positive pressure breathing with mask or bag or tracheostomy; ceftriaxone 25 mg/kg to 1 g i.v. once daily for 5 d or cefotaxime 25 mg/kg to 1 g i.v. 8 hourly for 5 d or (if severe penicillin hypersensitivity) chloramphenicol 50 mg/kg to 1 g i.v. immediately, followed by 25 mg/kg to 1 g i.v. 8 hourly

Diphtheria: antitoxin + parenteral penicillin

Prophylaxis

***Haemophilus influenzae* type b:** given to index case before discharge, and within 7 d to all household contacts of index case, including incompletely immunised children < 4y and any immunocmpromsed child; also adults and children at day care centres with 2 or more cases of invasive disease in 60 d period and with incompletely immunised children; rifampicin 20 mg/kg to maximum 600 mg (child < 1 mo: 10 mg/kg) orally daily for 4 d (not pregnant; give ceftriaxone 1 g in lignocaine hydrochloride 1% i.m. as single dose); vaccine to index case under 2 y even if previous immunisation and to unvaccinated contacts < 5 y; all children should be routinely vaccinated beginning at 2 mo (95-100% efficacy; swelling, redness and pain at injection site in 5-30%, fever and irritability uncommon, serious reactions rare; contraindicated if anaphylaxis to vaccine components or previous dose and serious illnesses)

Neisseria meningitidis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral

contraceptive), rifampicin 10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

Acute Tracheitis: secondary bacterial infection following primary viral respiratory infection, most commonly parainfluenza

Agents: *Staphylococcus aureus, Haemophilus influenzae, Streptococcus pyogenes, Moraxella catarrhalis, Acinetobacter calcoaceticus, Bordetella bronchiseptica* (rare), 1 case of *Corynebacterium pseudodiphtheriticum*

Diagnosis: URTI with stridor, fever and variable degree of respiratory distress; Gram stain and culture of tracheal aspirate

Treatment: humidification, endotracheal intubation or tracheostomy; amoxycillin-clavulanate

Upper Airways Aspergillosis: necrotising bronchitis, mass in trachea, laryngitis, epiglottitis

Agents: *Aspergillus* species

Diagnosis: fibreoptic examination; micro and culture of biopsy

Treatment: amphotericin B; excision possibly helpful; removal of infected suture essential for bronchial stump aspergillosis

Whooping Cough: world-wide; acute tracheobronchitis, mainly in children, sometimes in elderly whose immunity has waned; also common cause of persistent cough in adults; ≈ 4000 notified cases/y in Australia (≈ 32% in New South Wales); incidence 0.8/100 000 in USA; 0.3% of new episodes of illness in UK; death rate from 0.003/1000 infants in USA to 5/1000 in Guatemala; case-fatality rate 0.5-15% (29% pneumonia, 4% seizures, 0.4% encephalopathy; all < 1 y, unvaccinated; ≈ 300,000 deaths in children worldwide in 2000); complications include inguinal or umbilical hernia, rectal prolapse, mucosal hemorrhage, petechiae, pneumothorax (rare), subcutaneous emphysema (rare), subdural haematoma (rare), convulsions, paralysis, deafness, blindness, aphasia, mental retardation, bronchopneumonia, atelectasis, ? bronchiectasis; respiratory transmission; incubation period 5-10 d, latent period 6-7 d, infectious period 21-28 d, interepidemic period 2-5 years

Agents: *Bordetella pertussis* (pertussis, chin cough, morbus cucullaris; acute respiratory disease, common in childhood), *Bordetella parapertussis* (parapertussis; less common and usually mild respiratory disease), *Bordetella bronchiseptica* (uncommon acute tracheobronchitis); parainfluenza 4 and adenovirus may produce a similar syndrome

Diagnosis: initial stage of mild upper respiratory symptoms, followed by a second stage of paroxysmal coughing, with each paroxysm ending (but not invariably, especially in infants) in an inspiratory 'whoop' and post-tussive vomiting, and a long period of convalescence; fever usually absent or of low grade; may be transiently indistinguishable from adenoviral respiratory diseases; cough ≥ 14 d duration (CDC definition) has 100% sensitivity but only 35% specificity; spasmodic cough ≥ 21 d (WHO definition) has 80% sensitivity but only 41% specificity; ≥ 14 d cough + lymphocytosis has sensitivity 84%, specificity 67%, predicted value positive 68%; culture of nasopharyngeal swab plated directly to charcoal agar + antibiotics (overall sensitivity 53%, specificity 100%; the organism does not survive transport in Stuart's medium even for a few minutes; the chance of isolating the organism falls rapidly from 93% at time of onset to zero at > 4 w after onset); serology (IgA or rise in IgG or IgM); PCR on nasopharyngeal swab or aspirate; direct fluorescent microscopy of organisms in sputum (sensitivity 63%, specificity 86%); ELISA (IgG for filamentous haemagglutinin sensitivity 88-89%, detects both *Bordetella pertussis* and *Bordetella parapertussis*; IgG for pertussis 100% sensitive in unvaccinated children, specificity 97%; IgA); neutropenia becoming lymphocytosis

Treatment: mainly supportive, but clarithromycin 7.5 mg/kg to 500 mg orally twice daily for 7 d (not < 1 mo), azithromycin 10 mg/kg to 500 mg initially then 5 mg/kg to 250 mg orally daily for further 4 d (< 6 mo: 10 mg/kg to 500 mg orally daily for 5 d), erythromycin 10 mg/kg to 250 mg orally 6 hourly for 7 d (not < 1 mo), erythromycin ethyl succinate 10 mg/kg to 400 mg orally daily for 7 d (not < 1 mo), or cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly for 7 d may shorten the course of the disease if treatment is initiated very early and may limit spread to susceptible contacts

Prophylaxis: vaccine (3 doses) 70% effective; 50% minor complications (40% swelling, 35% redness, 35% irritability, 30% pain, 25% fever ≥ 38°C, 15% anorexia, 15% drowsiness, 5% fever ≥ 39°C, 1% fever ≥ 40°C), 0.03% moderate complications, 0.003% severe complications (70-2000/M persistent screaming, 60-300/M collapse or shock, 40-700/M convulsions ± fever), 0.0006% encephalitis (males predominate; not related to age at immunisation, size of dose or whether first or subsequent dose; manifestations: changes in consciousness, convulsions, paresis; mortality ≈ 15%; permanent sequelae ≈ 30%); paracetamol 15mg/kg at time of vaccination

and every 4-6 h for 48-72 h reduces incidence of fever and seizures; further immunisation contraindicated if collapse or shock within 48 hours, persistent screaming episode or uncontrollable crying lasting ≥ 3 h within 48 hours, temperature ≥ 40.5°C within 48 h, convulsions ± fever within 3 d, alteration in consciousness or neurologic abnormality within 7 days, systemic allergic reaction, thrombocytopenia or hemolytic anemia following previous immunisations or if neurologic disease; duration of immunity 6 y; new acellular vaccine 87% fewer febrile episodes, 75% fewer hypotonic-hyporesponsive episodes; cost effective

Chemoprophylaxis: contacts with index case who are infants < 1 y regardless of immunisation status, children 1-2 y who have received < 3 doses of vaccine, women in last month of pregnancy, or who attend or work in a childcare facility; as for treatment

TRACHEOBRONCHITIS

Agents: parainfluenza 1, 2, 3, influenza A, B, adenovirus 1, 2, 3, 4, 5, 7; also *Bordetella* (see **WHOOPING COUGH**), *Mycoplasma pneumoniae*, *Aspergillus* (ulcerative and plaque-like in AIDS patients; see **UPPER AIRWAYS ASPERGILLOSIS**)

Diagnosis: bronchoscopy; serology; culture of biopsy

Treatment: steam, hydration

EPIDEMIC INFLUENZA: 20% of acute illness (≈ 20 000 deaths/y) in USA, 0.9% of new episodes of illness in UK; causes 5% of fever in returned travellers to Australia; attack rate 34%, case-fatality rate 0.9%; particularly severe in those in third trimester of pregnancy, in elderly, in patients with underlying cardiovascular disease, renal disease, metabolic diseases such as diabetes mellitus, anemia, and in immunosuppression; initial pneumonitis often progresses to secondary bacterial pneumonia, often due to *Haemophilus influenzae* but particularly severe form due to *Staphylococcus aureus*; common complications include pneumonia, otitis media, tracheobronchitis and acute sinusitis; others include Reye's syndrome, myocarditis, pericarditis, myositis, myoglobinuria, encephalitis, transverse myelitis, Guillain-Barré syndrome, rhabdomyelitis, respiratory transmission; incubation period 1-4 d

Agents: 70% influenza A (world-wide epidemics and pandemics), 27% influenza B (smaller epidemics), 3% influenza C (local outbreaks, often inapparent); 'influenza-like illness' also occurs with infections due to adenovirus, enteroviruses, parainfluenza, hepatitis C, Q fever, Rift Valley fever, Ross River virus, lymphocytic choriomeningitis virus, and in malaria, perfringens poisoning (mild, lasting 24 h), rabies, staphylococcal food poisoning, as well as in rifampicin overdosage

Diagnosis: abrupt onset of fever, chills, severe myalgia, severe arthralgia, anorexia, severe headache, severe malaise, severe nonproductive cough, severe chest discomfort, fatigue lasting 2-3 w; viral culture of oropharyngeal or nasopharyngeal swab or garglings, sputum, serum (lung tissue post mortem) in chick embryo amnion, human, monkey, pig or calf kidney cells; serology (complement fixation test, microagglutination, indirect fluorescent antibody titre, passive hemagglutination, hemagglutination inhibition antibody, neutralisation, ELISA (antibody), radioimmunoassay); sensitivity of rapid commercial kits 51-96% (greater with nasopharyngeal specimen), specificity 52-100% (influenza A and B); relative or absolute lymphocytosis with neutropenia, becoming neutrophilia if secondary bacterial infection

Treatment:

Influenza (High Risk Individual in Context of Proven Influenza Epidemic and Within 48 Hours of Onset of Illness): zanamivir 10 mg by inhalation 12 hourly for 5 d or until 48 h after recovery (not < 7 y) or oseltamivir (≤ 15 kg: 30 mg; 16-23 kg: 45 mg; 24-40 kg: 60 mg; > 40 kg: 75 mg) orally twice daily for 5 d (influenza A and B)

Q fever: doxycycline 100 mg orally 12 hourly for 14 d (not < 8 y), chloramphenicol 12.5 mg/kg to 500 mg orally or i.v. 6 hourly for 14 d

Others: symptomatic

Prophylaxis (Influenza A and B): vaccination + rimantidine most cost-beneficial; killed vaccine administered parenterally 77-91% efficacy in children 1-15, 70-90% in adults < 65 y, 50-80% in ≥ 65 y, rare systemic reactions, duration of immunity 1-3 y; persons at increased risk (aged ≥ 50 y; children 6-59 months; residents of nursing homes and other chronic care facilities; ≥ 6 mo with chronic disorders of pulmonary (including asthma) or cardiovascular systems (not including hypertension); ≥ 6 mo who have required regular medical follow-up or hospitalisation during preceding year for chronic metabolic diseases (including diabetes mellitus), renal dysfunction, haemoglobinopathies or immunodeficiency caused by medications or HIV; aged 6 mo - 18 y and receiving long term aspirin therapy; ; ≥ 6 mo with any condition that can compromise respiratory function or handling of respiratory secretions or increases risk for aspiration, cognitive dysfunction, spinal cord

injuries, seizure disorders or other neuromuscular disorders; women who will be pregnant during the influenza season) and groups with potential of nosocomially transmitting influenza to high-risk patients (physicians, nurses and other personnel in both hospital and outpatient care settings, including emergency response workers; employees of nursing homes and chronic care facilities who have contact with patients or residents; employees of assisted living and other residences for persons in groups at high risk; persons who provide home care to persons in groups at high risk; individuals who live with or care for high-risk individuals, including healthy household contacts and caregivers for children age 0-59 mo) should be immunised each year, 1-2 mo before expected epidemic; also consider for overseas travellers; group vaccination of school-aged children highly cost effective; not recommended if < 6 mo age; 6 mo - 3 y: 2 x 0.25 mL doses split virus; 3-8 y: 2 x 0.5 mL doses split virus; ≥ 9 y: 1 x 0.5 mL dose whole or split virus; side effects: pain at injection site; fever, malaise, myalgia mainly in previous recipients;fever, rash and seizures in children 6-23 mo; Guillain-Barre syndrome 1/1M; allergic reactions to eggs or other components; increased side effects in asthmatic children, ? systemic lupus erythematosus; decreased response in malignancy patients on therapy, patients with chronic renal failure, and transplantation patients (particularly if azotemic), and in patients with systemic lupus erythematosus or with rheumatic diseases receiving corticosteroids; exercise improves response; cost saving relative to oseltamivir or supportive care; live attenuated vaccine administered intranasally (5-8 y: 1 or 2 doses; 9-49 y: 1 dose; efficacy 86-93% in healthy children, 71-85% in healthy adults) may be given to those not on above list (not immunosuppressed, pregnant or with prior history of Guillain-Barre syndrome); amantadine and rimantidine give similar, but probably inferior, protection (influenza A only); oseltamivir (≤ 15 kg: 30 mg; 16-23 kg: 45 mg; 24-40 kg: 60 mg; > 40 kg: 75 mg) orally once daily during influenza season (≥ 13 y; 84% efficacy; cost saving relative to supportive care alone); zanamivir 10 mg 2 inhalations twice daily (not < 5 y) to prevent spread within families

ACUTE CHEST INFECTIONS

Agents

<4 y: 33% respiratory syncytial virus, 13% influenza A and B, 9% parainfluenza 1, 2 and 3, 5% adenovirus, 5% *Mycoplasma pneumoniae*, 2% coronavirus, 2% *Simplexvirus*, 8% mixed infections, 25% unknown

4-8 y: peak incidence; 'acute wheezy chest' (acute diffuse bronchitis with airway obstruction), segmental pneumonia, acute bronchiolitis; agents as for conditions listed

Diagnosis: acute wheezing common with respiratory syncytial virus; Gram stain, bacterial and viral culture and immunofluorescence of sputum, pharyngeal aspirate and nasopharyngeal aspirate; Becton Dickinson Directigen RSV on nasopharyngeal wash or aspirate sensitivity 93-97%, specificity 90-97%; serology

Treatment: ampicillin, cotrimoxazole; humidified oxygen; bronchoscopic suction or tracheostomy

BRONCHITIS: 2% of new episodes of illness in UK; 9-30 M cases in USA; acute bronchitis (0.4% of ambulatory care visits in USA) develops as a sequel to an acute upper respiratory infection, usually of viral origin; in chronic bronchitis (1.4% of ambulatory care visits in USA), there is almost daily production of sputum for 3 consecutive months over 2 consecutive years; 90% of chronic obstructive pulmonary disease (fourth leading cause of death in USA); acute exacerbations are common

Agents: viruses (*influenza A* and *B*, *respiratory syncytial virus*), nontypeable *Haemophilus influenzae* (13% of acute exacerbations of chronic obstructive pulmonary disease), *Streptococcus pneumoniae* (6% of exacerbations of chornic obstructive pulmonary disease), other streptococci, *Staphylococcus aureus, Moraxella catarrhalis* (4% of acute exacerbations of chronic obstructive pulmonary disease), *Escherichia coli* (in newborn and recurrent exacerbations of chronic), *Klebsiella pneumoniae, Pseudomonas aeruginosa* (6% of acute exaacerbations of chronic obstructive pulmonary disease), *Chlamydophila pneumoniae, Bordetella pertussis, Bordetella bronchiseptica, Streptobacillus moniliformis, Corynebacterium diphtheriae, Mycoplasma pneumoniae*, *Candida albicans*, mixed anaerobes

Diagnosis:

Acute: productive cough with sputum, restrosternal pain on coughing, fever; purulent sputum usually indicates secondary bacterial infection

Acute Exacerbation of Chronic: change in sputum colour, consistency and quality; increasing cough, often with development of dyspnoea; chest tightness; general fatigue; Gram stain, bacterial culture of sputum

Chlamydophila pneumoniae: culture, serology, PCR-EIA

Treatment: usually not required for acute bronchitis consequent on viral infection

***Haemophilus influenzae, Streptococcus pneumoniae*, Empirical Treatment of Acute Exacerbation of Chronic With Increased Dyspnoea and Increased Sputum Purulence and Volume**: povidone iodine gargles may be as effective as antibiotics; amoxycillin 15 mg/kg to 500 mg orally 8 hourly for 5 d, doxycycline 4 mg/kg to 200 mg orally statim followed by 2 mg/kg to 100 mg orally daily for 5 d (not < 8 y, pregnant or breastfeeding); if amoxycillin resistant *Haemophilus influenzae* isolated, amoxycillin-clavulanate 500/125 mg orally 8 hourly (< 40 kg: 40/10 mg/kg daily in 3 divided doses) for 10-14 d; if unsatisfactory clinical response, ensure optimal physiotherapy and bronchodilator use, review diagnosis and perform chest X-ray

Resistant *Streptococcus pneumoniae:* clindamycin, grepafloxacin, levofloxacin, sparfloxacin, trovafloxacin

Chlamydia, Mycoplasma: tetracycline

Bordetella: erythromycin

Other Bacteria: amoxycillin-clavulanate or cefuroxime + bromohexine or N-acetylcysteine

Prophylaxis: oxytetracycline

BRONCHIECTASIS

Agents: viruses, *Haemophilus influenzae, Streptococcus pneumoniae*, *Pseudomonas aeruginosa*

Diagnosis: Gram stain and culture of sputum

Treatment:

Pseudomonas aeruginosa: oral ciprofloxacin + inhaled tobramycin

Others: ampicillin, tetracycline, erythromycin

ACUTE BRONCHIOLITIS AND BRONCHOPNEUMONIA: infants < 6 mo

Agents: respiratory syncytial virus (in 84% of cases), parainfluenza 1 and 3, influenza A and B, human metapneumovirus (in 59-68% of cases), *Streptococcus pneumoniae,* coliforms, *Mycoplasma pneumoniae, Bordetella bronchiseptica*

Diagnosis: expiratory wheezing (more common with respiratory syncytial virus) ± fine crepitation ± tachypnoea, air trapping or chest wall retraction; no significant response to bronchodilator; immunofluorescent smear of pharyngeal aspirate; bacterial and viral culture of nasopharyngeal aspirate, pharyngeal swab and sputum (lung, trachea, blood post mortem); ELISA, RIA, serology; PCR

Treatment: clarithromycin; dexamethasone 1 mg/kg single oral dose if < 2 y

Prevention (Respiratory Syncytial Virus): humanised monoclonal antibody (palivizumab)

BRONCHOPULMONARY CANDIDIASIS

Agent: *Candida albicans*

Diagnosis: lower lobe consolidation with repeated isolation of *Candida albicans* from sputum or single isolation from uncontaminated bronchial specimen; serology (immunodiffusion, latex agglutination, counterimmunoelectrophoresis)

Treatment: nystatin aerosols + amphotericin B

PNEUMONIA: fifth leading cause of death, first among infectious diseases; 3% of acute illnesses in USA (≈ 45,000 deaths/y; 0.5% of ambulatory care visits); 0.1% of new episodes of illness in UK; 20/1000 in < 1 y, 40/1000 in 1-5 y (90% viral)

Agents: mainly indigenous flora; 35-75% unknown aetiology, 6% aspiration, 3% postobstructive, 1% noninfectious; *Mycoplasma pneumoniae* (Eaton agent pneumonia, Eaton pneumonia, *Mycoplasma* pneumonia, mycoplasmal pneumonia, pleuropneumonia-like-organism pneumonia, PPLO pneumonia; 33% of community acquired bacterial pneumonia, 1% of community acquired pneumonia requiring ICU admission; deaths related to ineffective initial therapy, non-pneumonia related complications; world-wide, sporadic, endemic and occasionally epidemic), *Streptococcus pneumoniae* (320,000-620,000 hospitalisations/y in USA in > 65 y; 36% of community acquired and 50% of hospital-acquired bacterial pneumonia in adult; common, world-wide; increased risk in AIDS, immunosuppressive therapy, severe combined immunodeficiency, nephrotic syndrome, myeloma, chronic lymphocytic leukemia, common variable immunodeficiency, X-linked agammaglobulinemia; mortality rate from 1% in patients 20 y treated with penicillin to 70% in patients > 70 y not treated), *Chlamydiophila psittaci* from birds, *Chlamydophila pneumoniae* 9% of community acquired pneumonia, *Chlamydia trachomatis* usual cause in infants < 20 w during spring, summer and autumn, *Haemophilus influenzae* (7% of community acquired bacterial pneumonia; nontypeable strains in adults suffering from some predisposing respiratory tract disease such as chronic bronchitis or with chronic alcoholism or malignancy or B cell disease or not otherwise predisposed, and in

children, either primary (type b; 4 mo – 4 y; rates greatly decreased with Hib immunisation) or secondary to fibrocystic disease; rates greatly decreased with Hib immunisation), Gram negative bacilli (5% of community acquired pneumonia; increased risk in neutropenia, chronic granulomatous disease; coliforms result of antibiotic treatment or aspiration and in neutropenics; *Klebsiellla* 12% of nosocomial pneumonia; *Klebsiella pneumoniae* 10% of community acquired bacterial pneumonia requiring ICU admission, with 46% of these fatal, lower respiratory tract infection common, necrotising pneumonia caused by certain biochemically atypical strains uncommon, adult mortality rate 25-50%; *Enterobacter* 9% of nosocomial pneumonia; *Serratia* 6% of nosocomial pneumonia; *Escherichia coli* 6% of nosocomial pneumonia, common in neonatal; *Proteus* 4% of nosocomial pneumonia; *Pseudomonas* 17% of nosocomial pneumonia; *Pseudomonas aeruginosa* as for coliforms but mucoid strains in cystic fibrosis, 10% of ventilator associated pneumonia, rare cases of necrotising community-acquired pneumonia in immunocompetenet, adult mortality rate 35-80%; *Burkholderia cepacia*, *Stenotrophomonas maltophilia* following hospitalisation and antibiotic therapy; *Stenotrophomonas maltophilia* 15% of ventilator associated pneumonia; *Acinetobacter baumannii* 27% of ventilator associated pneumonia), *Staphylococcus aureus* (3% of community acquired bacterial pneumonia, 8% of community acquired pneumonia requiring ICU admission, with 50% fatal in these cases; 13% of nosocomial pneumonia; 24% of ventilator associated pneumonia; secondary to viral infection and in neutropenia and chronic granulomatous disease; adult mortality rate 10-20%; enterotoxin B aerosol possible biowarfare agent), *Legionella pneumophila* (from soil, water-cooling equipment; 3% of pneumonia cases (0-50% of nosocomial, with 40% mortality); ≈ 300 notified cases/y in Australia; incidence 0.2/100,000 in USA; incubation period 2-10 d; immunocompromised patients (AIDS, chemotherapy, radiation therapy, corticosteroids, underlying immune deficiencies), dialysis patients, late middle-aged to elderly males, chronic underlying disease (organic heart disease, lung disease, renal disease, diabetes), alcoholics and smokers; 5% of community acquired pneumonia requiring ICU admission (20% mortality)), *Legionella micdadei* (Pittsburgh pneumonia, nosocomial pneumonia, particularly in renal transplant and bone marrow transplant recipients), *Streptococcus pyogenes* (in neutropenics), other streptococci (30% of community acquired pneumonia requiring ICU admission, with 19% of these fatal; *Streptococcus agalactiae* (neonates), *Streptococcus milleri,* group C *Streptococcus* (mainly *Streptococcus equisimilis*) rare secondary to tonsillitis and bronchitis, viridans streptococci in neutropenia and chronic granulomatous disease), *Staphylococcus epidermidis* (relatively common nosocomial in neonates), *Mycobacterium tuberculosis* (increased risk in AIDS, immunosuppressive therapy, severe combined immunodeficiency), anaerobes (87% of cases of aspiration pneumonia—50% alone, 50% in combination with aerobes; also necrotising pneumonia—6% mortality; 34% *Fusobacterium nucleatum,* 31% *Prevotella melaninogenica,* 26% microaerophilic streptococci, 21% *Bacteroides fragilis*, 19% *Peptostreptococcus*, 16% *Prevotella oralis*, 15% *Peptococcus*; also *Bacteroides ureolyticus,* other *Prevotella*), uncommon cases due to actinomycetes, *Bordetella bronchiseptica, Haemophilus parainfluenzae,* anthrax (from cattle, swine, horses, wool, hides), *Brucella* (abattoir workers, veterinarians), *Coxiella burnetii* (from goats, cattle, swine), melioidosis (travel to SE Asia, S America), plague (from squirrels, chipmunks, rabbits, rats), tularemia (from rabbits, squirrels, infected fleas or ticks), leptospirosis (from rats, dogs, cats, cattle, swine), *Neisseria meningitidis* (6% of meningococcal infections; occasionally arising as result of spread from meningococcal nasopharyngitis; increased risk in nephrotic syndrome, myeloma, lymphocytic leukemia, immunosuppressive therapy, AIDS, common variable immunodeficiency, X-linked agammaglobulinemia), *Neisseria mucosa*, *Neisseria sicca, Moraxella catarrhalis*, *Chromobacterium violaceum* (in 33% of infections due to this agent), *Clostridium botulinum*, *Vibrio vulnificus* (in drowning victim), *Acinetobacter* (multiple clinical risk factors, especially cigarette smoking and alcoholism; 66% mortality), enterococci, *Corynebacterium pseudodiphtheriticum* (in trauma and immunodeficient), *Salmonella* (in renal transplant recipients), *Actinobacillus actinomycetemcomitans*, *Alcaligenes faecalis*, *Achromobacter xylosoxidans*, *Erwinia herbicola, Aeromonas hydrophila, Pasteurella multocida* (chronic), *Haemophilus aprophilus*, *Streptobacillus moniliformis, Veillonella parvula* (rare), *Enterococcus*, *Listeria monocytogenes*, *Ureaplasma urealyticum*, pertussis, *Rhodococcus equi* in immunocompromised, *Lactobacillus* (ventilator associated); also in 52% of cases of Q fever (febrile, sudden onset); viruses (influenza common in adults, infrequent in children; influenza A and B 47% of community acquired viral pneumonia (10% of total cases in season; influenza A 1% of total adult cases, influenza B 3%; influenza B in 3% of infected pre-school children and 1% of infected young adults; *human human cytomegalovirus* 26% of community acquired viral pneumonia, in AIDS, bone marrow and organ transplant recipients and others with impaired cell-mediated immunity; parainfluenza 21% of community acquired viral pneumonia; parainfluenza 1, 0.5% of cases in adults; parainfluenza 3, 4%; common in children, 19% of cases in infants; respiratory syncytial virus 3% of community acquired viral pneumonia (increased risk in AIDS, immunosuppressive therapy, severe combined immunodeficiency); adenovirus (1,

2, 3, 5, 7, 21) 3% of adult cases, 2-24% in children; varicella-zoster 0.5% of adult cases, in impaired cell-mediated immunity and normal adults; *Simplexvirus* in impaired cell-mediated immunity; measles; coxsackievirus A7, A9, B1; echovirus 9, 11 (exanthem); parvovirus B19; Mimivirus; rarely other viruses); *Aspergillus* and *Candida* (long-term intravenous catheterisation and broad spectrum antibiotics, neutropenia, chronic granulomatous disease), *Coccidioides immitis* (may present with interstitial granulomatous dermatitis), *Cryptococcus neoformans* (increased risk in AIDS, immunosuppressive therapy, severe combined immunodeficiency), *Histoplasma capsulatum, Mucor, Curvularia lunata* (rare); *Pneumocystis jiroveci* (3-4% of community acquired pneumonia; 0.5% of adult cases; increased risk in AIDS, immunosuppressive therapy, severe combined immunodeficiency), *Paragonimus, Toxoplasma*, *Strongyloides stercoralis* (AIDS, immunosuppressive therapy, severe combined immunodeficiency), other parasites; predisposing factors include congenital anomalies (cleft palate, tracheoesophageal fistula, sequestration of lung), congenital or acquired immune defects, alteration in level of consciousness (seizures, stroke, anesthesia, intoxication, trauma), depressed pulmonary clearance (cigarette smoke, hypoxemia, acidosis, ethanol, uremia), steroids and immunosuppressive agents, mechanical obstruction

Diagnosis: chills, fever, headache, malaise, fatigue, cough (bacterial: productive; viral: non-productive, hoarse, paroxysmal), tachypnea ± chest wall retraction, fine to medium crepitation (rales) on auscultation; evidence of pulmonary infiltration or consolidation on chest X-ray; sputum Gram stain and culture low diagnostic yield

Bacterial: causes 6% of fever in returned travellers to Australia; sudden onset, severe toxicity, signs of consolidation on physical common, rigours common, high fever (> 39°C), purulent sputum with neutrophils and abundant bacteria on Gram stain, pleuritic chest pain common, white cell count elevated with immature neutrophils, consolidation on X-ray; blood cultures; aspartate and alanine aminotransferase (levels increased with *Legionella, Chlamydia psittaci, Coxiella burnetii*), serum phosphorus (slightly decreased with *Legionella*), erythrocyte sedimentation rate or C-reactive protein (highly elevated in legionnaires disease)

Streptococcus pneumoniae: abrupt onset of variable fever of 38-41°C usually sustained, severe rigours, usually single, shaking chills at onset, productive cough, pleuritic chest pain, productive cough of mucopurulent or rusty (bloody) sputum, shortness of breath, hypoxia, tachypnea, malaise, nausea, vomiting, headache; preceding upper respiratory infection common; herpes labialis frequent; diminished breath sounds, dullness to percussion, crackling, bronchial breath sounds; massive consolidation of entire lung; multilobar involvement in 10-30%; pleural effusion uncommon; empyema in 2%, pericarditis, atelectasis, lung abscess other complications; Gram stain (Gram positive diplococci), semi-quantitative microscopy-directed culture and coagglutination (sensitivity 82-93%, specificity 89%) of carefully collected sputum; rapid immunochromatographic membrane test on urine (sensitivity 66-70%, specificity 90-100%); counterimmunoelectrophoresis (serum sensitivity 45-80%, urine sensitivity 50-66%, sputum sensitivity 27-100%, pleural fluid sensitivity 100%); ELISA; blood urea ≥ 7 mmol/L in 55% of cases, liver function tests abnormal in 24%, serum sodium ≤ 130 mmol/L in 23%, serum albumin ≤ 2.5 g/dL in 41%, white cell count ≥ 15,000/μL with left shift in 40%

Other Streptococci: hectic fever of 40°C or higher, multiple rigours, productive cough, pleuritic chest pain; purulent sputum, may be blood-streaked, Gram positive cocci in chains in Gram stain; white cell count 20,000-30,000/μL with left shift; pleural effusion and empyema common; often follows influenza

Legionnaires' Disease (Broad Street Pneumonia, Legionellosis, Legionnaires Pneumonia): world-wide; ≈ 250 notified cases/y in Australia; often derived from showers and water cooling towers, also other industrial, commercial, hospital and domestic environmental sources; no person-to-person transmission; incubation period 2-10 d; risk factors older age, male, heavy smoker, underlying disease associated with immunodeficiency; characterised by extensive inflammation of pulmonary alveolar tissue, often hemorrhagic, with many intra- and extracellular bacilli present in alveoli and respiratory bronchioles; clinical manifestations range from nonprogressive pneumonia with a minimum of extrapulmonary involvement to severe pneumonia with rapidly progressive pulmonary infiltration, severe hypoxia and respiratory failure, with, in many cases, multi-organ dysfunction, including neurological symptoms with frequent central nervous system abnormalities, renal involvement (hematuria, oliguria, proteinuria, renal failure), severe myositis (elevated creatine kinase and lysine dehydrogenase), anemia, hepatic abnormalities (elevated aspartate aminotransferase and bilirubin), high frequency of band neutrophils, and gastrointestinal symptoms; presence of prodromal 'viral-like' illness, dry cough, confusion, diarrhoea, lymphopenia without neutropenia, hyponatremia most useful symptoms; flu-like symptoms, malaise, fever of 39.5-41°C, multiple rigours, shaking chills, nonproductive cough, pleuritic chest pain, tachypnea, rales, sputum mucoid (if present) with rare polys and mononuclear cells and no bacteria on stain, myalgias and arthralgias, watery diarrhoea in 50%, abdominal distension, abdominal pain, nausea and vomiting, relative bradycardia,

headache, confusion, disorientation, delirium, hepatomegaly, dense airspace opacification of upper and lower lobes, patchy infiltrates to frank consolidation on X-ray; culture of sputum, bronchoalveolar lavage, bronchoscopy material, transtracheal aspirate, lung tissue, pleural fluid or blood on charcoal yeast extract agar with and without decontamination with KCl-HCl (sensitivity 80%, specificity 100% but ≈ 1/3 of laboratories incapable of growing organism; turnaround time 3-5 d); detection of specific antigen in respiratory secretions or urine; direct fluorescent (within first 9 d of therapy; sensitivity 25-75%, specificity > 95%; turnaround time 12 h) and indirect fluorescent antibody testing (rise in titre to at least 1:128; sensitivity 60-80%; results may be delayed > 2 mo) of transtracheal aspirate, fresh lung scrapings; radioimmunoassay or enzyme immunoassay of urine (early in disease; sensitivity 85%, specificity 100%; *Legionella pneumophila* serotype 1 only; 24 h turnaround time; positive for days to weeks after initiation of antibiotics); 4X serum antibody rise on complement fixation test (other than serogroup 1; sensitivity 40-60%, specificity 96-99%; turnaround time 24 h) or by direct immunofluorescent antibody test or microagglutination (serogroup 1); immunoalkaline phosphatase staining of lung tissue; polymerase chain reaction of respiratory specimens; blood urea ≥ 7 mmol/L in 58% of cases, liver function tests abnormal in 79%, serum sodium ≤ 130 mmol/L in 53% (syndrome of inappropriate ADH secretion), serum albumin ≤ 2.5 g/dL in 47%, white cell count ≥ 15,000/μL in 84% (mean 18,000/μL, 78% neutrophils, 15% lymphocytes, 7% monocytes, 50% with left shift), pO_2 53 mm Hg; lumbar puncture studies normal

Staphylococcus aureus: more common in neonates and infants < 12 mo; hectic or sustained fever of 39-41°C, multiple rigours, productive cough, pleuritic chest pain; purulent sputum, may be blood-streaked; Gram positive cocci in clusters on Gram stain; white cell count > 15,000/μL with left shift; affects infants, elderly, debilitated, may follow influenza; alveolar disease, pneumatocoeles, empyema, nonspecific pulmonary infiltrate, massive consolidation, lung abscess common; counterimmunoelectrophoresis of pleural fluid (sensitivity 86%)

***Staphylococcus aureus* Enterotoxin B:** incubation period < 4 h; fever (up to 41.1°C) myalgias, headache; respiratory symptoms (dry, non-productive cough, dyspnea, orthopnea, chest pain, crackles) begin ≈ 10 h after exposure; detection of toxin with ELISA or PCR on urine within several hours or in nasal swabs within 24 h

Klebsiella pneumoniae: fever of 38-39°C, multiple rigours, productive cough, pleuritic chest pain; mucopurulent sputum, may be bloody, Gram negative bacilli with thick capsules in Gram stain; white cell count 20,000-40,000/μL with left shift; affects upper lobes, dense infiltrate, abscesses, heavy exudate in lung parenchyma causing downward bulging of horizontal pulmonary fissure, cavitation in 3-5 d of infection; seen in diabetics, alcoholics and patients with chronic lung disease; counterimmunoelectrophoresis of serum (sensitivity 100%), pleural fluid (sensitivity 50%)

Anaerobes: 74% suspected aspiration, 70% pulmonary infection characterised by parenchymal necrosis, 57% subacute or chronic presentation, 53% putrid discharge; fever variable, often low grade, rigours infrequent, productive cough; sputum purulent and foul-smelling, with mixed flora on Gram stain; white cell count variable; associated with periodontal disease and altered state of consciousness; consolidating infiltrate in right lower lobe or upper lobes; lung abscess, empyema common; pulmonary specimens should be obtained by percutaneous transtracheal aspiration, direct lung puncture or double catheter and bronchial brush bronchoscopic specimen; pleural specimens should be obtained by thoracentesis

Pseudomonas aeruginosa: counterimmunoelectrophoresis of serum (sensitivity 100%)

Chlamydophila pneumoniae: mild; mean white cell count ≈ 9100/μL; isolation, microimmunofluorescent antibody, PCR-EIA

Chlamydia trachomatis: conjunctivitis, tachypnea, inspiratory crackles, failure to thrive; diffuse interstitial infiltrates with hyperaeration, peribronchial thickening, scattered areas of atelectasis

Haemophilus influenza: consolidative pneumonia and pleural involvement; isolation from pleural fluid

Other Gram Negative Bacilli: usually high fever, may be absent in elderly, debilitated; multiple rigours; productive cough; purulent sputum, Gram negative bacilli in Gram stain; white cell count variable; affects infants, elderly, debilitated, alcoholics, diabetics, those on antibiotics, steroids or immunosuppressive agents, ventilators; chest CT to exclude underlying fungal cause

Pulmonary Anthrax: incubation period 1-60 d; at first (1-6 d post-exposure), mild signs of upper respiratory tract involvement (fever and chills, malaise, fatigue and lethargy in all, minimal nonproductive cough in 90%, nausea or vomiting in 90%, dyspnea in 80%, sweats, often drenching, in 80%, mild chest discomfort

or pleuritic pain in 70%, myalgias in 60%, headache in 50%, confusion in 40%, abdominal pain in 30%, sore throat in 20%, rhinorrhea in 10%; tachycardia, high hematocrit, low albumin and sodium); then, after a few days, several hours to days of improvement, followed by abrupt development of severe respiratory distress, hypoxia, dyspnea, cyanosis, stridor, high temperature, profuse sweating, with shock and death usual within 24-36 h; mediastinal widening with pleural effusions but without infiltrates on X-ray (computed tomography if inconclusive); Gram stain and culture of nasopharyngeal swab within 48 h of exposure, sputum, pleural fluid later; blood cultures; PCR of pleural fluid or blood if available; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test; 86% case-fatality rate

Pneumonic Plague: incubation period 1-6 d; severe, rapidly progressing pneumonia; fever, dyspnea, chest pain, cough with bloody, watery or purulent sputum, nausea, vomiting, diarrhoea, abdominal pain, hypotension, altered mentation, oliguria, rarely cervical buboes; WCC 10,000-20,000/µl with neutrophils predominant and toxic granulations; elevated liver enzyme levels; coagulopathy; disseminated intravascualr coagulation in severe cases; culture of blood, sputum or aspirates; direct fluorescent antibody staining, dipstick antigen detection tests; rapid monoclonal antibody test (sensitivity 100%, specificity 100%, positive predictive value 91%, negative predictive value 87%)

Tularemia: severe atypical pneumonia often confused with legionellosis; incubation period 1-14 d followed by influenza-like illness with fever (38-40°C), chills, rigours, myalgias, anorexia, sore throat, cough (usually non-productive), pleuritic chest pain, substernal tightness, dyspnea and pharyngitis; parenchymal infiltrates with patchy, ill-defined and multi-lobar opacities in 74%, pulse-temperature dissociation in nearly half, erythema nodosum, erythema multiforme or maculopapular, vesicular or urticarial rash in 35%, pleural effusions in 20-55%; leucocytosis in 25-42%, elevated transaminase levels, hyponatremia, elevated creatine phosphokinase level, pyuria, myoglobinuria; 35% fatality rate untreated; smear and culture positive in 5%; blood cultures often give false negative; serology, ELISA, immunofluorescence, PCR, antigen skin testing

Mycoplasmal: abrupt or slow onset, with malaise in 74-89% of cases and headache in 60-84%, followed a few days later by fever of 38-40°C in 96-100%, rales/wheezes in 80-84%, chilliness in 58-78%, sore throat in 53-71%, myalgias in 45%, chest discomfort in 42-69%, nasal stuffiness in 29-69%, cervical adenopathy in 18-27%, pharyngeal erythema without exudate in 12-73%, occasional rigours and paroxysmal cough, nonproductive in 93-100%; sputum mucoid if present, with rare polys and no bacteria in Gram stain; complications include skin rashes (usually maculopapular or urticarial, also Stevens-Johnson syndrome and erythema nodosum), otitis (including bullous hemorrhagic otitis), urethritis, glomerulitis, pleurisy, pneumothorax, hyperlucent lung syndrome, lung abscess, anemia (including hemolytic), thrombocytopenia, pericarditis, myocarditis, encephalitis/meningitis in 1/1000 cases (60% encephalitis/meningoencephalitis in slightly older patients; 10% mortality, 20% long term neurological morbidity; aseptic meningitis in younger age group; complete recovery with no neurological sequelae), poliomyelitis-like syndrome, Guillain-Barré syndrome, brain stem syndrome/cerebellar ataxia, psychosis; may be severe and rapidly progressive in children with sickle cell disease; incubation period 12-21 d; children and young adults (4-20 y); community acquisition; person-to-person transmission; 10-25% mild pleural effusion; physical unimpressive though X-ray shows patchy nodular infiltrates, bronchopneumonia often involving a single lower lobe, plate-like atelectasis or hilar adenopathy; lobar consolidation (alveolar-filling disease) rare; may have bullous myringitis; may be suggested by lack of response to penicillins and cotrimoxazole; bedside cold agglutination test 50% sensitivity but $\approx$ 100% specificity; rising titre of cold agglutinins (sensitivity 50%, specificity 50%); complement fixation test (2-3 w post onset; commercially available; 4X rise sensitivity 54%, not completely specific–may cross-react with *Legionella*); early IgM-ELISA (sensitivity 90%, specificity 75%); culture of bronchoalveolar lavage; all methods lack sensitivity and, except for the ELISA and bedside cold agglutination test if positive, are too slow to influence therapy; a commercially available DNA-RNA probe is very specific but sensitivity has varied between 22% and 100%); neutropenia with relative lymphocytosis becoming neutrophilia; white cell count > 15,000/µL in 87% of cases; myelocytes, metamyelocytes and plasmocytosis; raised ESR; hemolytic anemia occasionally; blood urea $\geq$ 7 mmol/L in 16%; serum sodium $\leq$ 130 mmol/L in 5%; serum albumin never < 2.5 g/dL

Differential Diagnosis: psittacosis, Q fever, viral pneumonia (adenovirus, rhinovirus, influenza B, parainfluenza 1, 2 and 3, enteroviruses, respiratory syncytial virus) and, occasionally, legionnaires disease (indirect immunofluorescence for antibody) and tularemia pneumonia (4X rise in direct agglutination test) may give similar symptoms; the 'group' term 'primary atypical pneumonia' is used but serves no useful purpose; other conditions that may mimic include *Pneumocystis jiroveci* pneumonia (in patients with

failure of the immune system due to AIDS, steroidal drugs or bone marrow depression), multiply resistant *Streptococcus pneumoniae, Pseudomonas* pneumonia (in granulocytopenia), *Haemophilus influenzae* pneumonia (in hypogammaglobulinemia), respiratory syncytial virus (ELISA for IgG and IgM antibodies), *human human cytomegalovirus* (4X rise in complement fixation test titre), *Ureaplasma urealyticum* (ELISA for IgG, IgM and IgA), *Chlamydia trachomatis* (rise in titre on serial microimmunofluorescence tests)

Ventilator Associated: quantitative endotracheal aspirate (10^5 cfu/ml; sensitivity 93%, specificity 80%) or bronchoalveolar lavage fluid culture; direct E-Test

Viral: incubation period 1-3 d; all ages; person-to-person transmission; underlying disease, smoking, alcohol in some cases; upper respiratory symptoms; pleural effusion rare; gradual onset, myalgia prominent, mild to moderate toxicity, minimal physical findings (consolidation rare), involvement on X-ray out of proportion to symptoms (usually patchy consolidation at bases of lungs, but also hyperexpansion, parahilar peribronchial infiltrates, atelectasis, hilar adenopathy; lower lobe and perihilar infiltrates in atypical measles and pneumonic infiltrate in one lobe in 2/3 of respiratory syncytial virus cases), rigours uncommon, low grade fever; sputum mucoid (if present) with mononuclear cells and rare bacteria on Gram stain; pleuritic chest pain uncommon; white cell count normal; complement fixation test for influenza A and B, parainfluenza 1 and 3, respiratory syncytial virus, adenovirus; also hemagglutination inhibition, neutralisation, ELISA; viral culture and immunofluorescence of nasopharyngeal aspirate, sputum, throat swab, lung biopsy

Influenza: fever of 39.5-40.5°C, rigours uncommon, nonproductive, hacking cough; headache, photophobia, myalgia, gastrointestinal complaints; sputum scant, may be bloody, rare polys and no bacteria in Gram stain; white cell count 10,000-15,000/μL; seen in patients with chronic lung and heart disease, pregnancy; profound dyspnea, cyanosis; seen in autumn and winter; adult mortality rate 80-90%; viral culture

Adenovirus: most common in < 18 mo; acute onset, high fever (> 39°C), rigours rare, persistent cough, sputum scant with no organisms or polys in Gram stain; associated with lethargy, diarrhoea, pharyngitis, severe conjunctivitis; epidemic in closed populations (up to 10% of military recruits infected; types 4 and 7; 90% of pneumonia hospitalisations); dyspnea, tachypnea, diffuse wheezing, crackles; diffuse bilateral infiltrates, interstitial and peribronchial, with hyperinflation and lobar collapse and hilar adenopathy, on X-ray; pleural effusions extremely rare; may progress to hepatosplenomegaly, myocarditis, nephritis, hematological abnormalities and a disseminated intravascular coagulation-like picture; mortality rate (type 7) ≈ 60% in immunocompromised and ≈ 20% in young infants; sequelae (bronchiolitis obliterans, bronchiectasis, unilateral hyperlucent lung) associated with abnormal pulmonary function in up to 60%; white cell count < 10,000/μL; direct fluorescent antibody staining of tracheal or nasopharayngeal aspirate

Echovirus: low grade fever, rigours rare, cough variable, sputum scant with no organisms or polys in Gram stain; white cell count < 10,000/μL; rash may be present; seen in summer

Respiratory syncytial virus: more common in winter; fever of 38-40°C in 60%, rigours rare, cough variable, frequent wheezing, sputum scant with no organisms or polys in Gram stain; white cell count 10,000-20,000/μL; seen primarily in children; X-ray changes often more severe than in other viral; direct fluorescent staining or ELISA on tracheal or nasopharyngeal aspirate; culture of tracheal aspirate

Parainfluenza: fever of 38-40°C, rigours rare, cough variable, may have 'croup'; sputum scant with no organisms or polys in Gram stain; white cell count < 10,000/μL; seen primarily in children; direct fluorescent antibody staining of tracheal or nasopharyngeal aspirate

Varicella: early in disease; fever up to 40.5°C; rigours rare, cough harsh and nonproductive; sputum scant, though may be bloody, no organisms in Gram stain; white cell count < 10,000/μL; rare in children; affects 15-30% of adults with varicella; nodular densities on X-ray, later calcify

Differentiation From Secondary Bacterial Pneumonia In Varicella: latter usually children < 7 y, late in disease, white cell count elevated with left shift, positive sputum and (occasionally) blood cultures, segmented or lobar infiltrate or consolidation

Human human cytomegalovirus: culture of tracheal aspirate

Pneumocystis jiroveci: Wright-Giemsa, Papanicolaou, methenamine silver staining, direct immunofluorescence of induced sputum (sensitivity 30-90%), bronchoalveolar lavage (sensitivity 98-100%), pulmonary biopsy (sensitivity 90-95%)

Paragonimus: Far East, Latin America; incidence 5M/y; abnormal chest X-ray (infiltration, cavities, pleural effusion) in 88% of cases; ova in sputum or feces; complement fixation test

Differential Diagnosis: pulmonary infarction, acute bronchitis, pulmonary tuberculosis, congestive heart failure, lung abscess

Treatment: supplemental oxygen, analgesia for pleuritic chest pain, bronchodilators to treat airflow limitation or to improve mucociliary clearance, physiotherapy, hydration, electrolytes, nutrition, control of co-morbidities as required

Community Acquired

Birth to 1 w: benzylpenicillin 60 mg/kg i.v. 12 hourly for 7 d + gentamicin (< 30 w gestation: 2.5-3 mg/kg; > 30 w gestation: 3.5 mg/kg) i.v. daily for 7 d

1 w to < 4 mo

Afebrile and Mildly to Moderately Ill: azithromycin 10 mg/kg orally daily for 5 d or clarithromycin 7.5 mg/kg orally 12 hourly for 7 d (not < 1 mo) or erythromycin 10 mg/kg orally or i.v. 6 hourly for 7-14 d (not < 1 mo) or erythromycin ethyl succinate 20 mg/kg orally 6 hourly for 7-14 d (not < 1 mo)

Febrile or *Chlamydia* Excluded: benzylpenicillin 30 mg/kg i.v. 6 hourly for 7 d

Severe Disease: cefotaxime 25 mg/kg i.v. 8 hourly for 7 d

4 mo to < 5 y

Mild: amoxycillin 25 mg/kg orally 8 hourly for 7 d

Moderate: benzylpenicillin 30 mg/kg i.v. 6 hourly for 7 d [if hospitalisation difficult, procaine penicillin (3 - < 6 kg: 250 mg; 6 - < 10 kg: 375 mg; 10 - < 15 kg: 500 mg; 15 - < 20 kg: 750 mg) i.m. daily for 5 d]

Severe:

Tropical Australia with Diabetes, Cystic Fibrosis, Congenital Heart Disease: meropenem 25 mg/kg to 1 g i.v. 8 hourly

Others: cefotaxime 25 mg/kg i.v. 8 hourly for 7 d, ceftriaxone 25 mg/kg i.v. daily for 7 d + di/flucloxacillin 50 mg/kg i.v. 6 hourly for 7 d

5-15 y

Mild: amoxycillin 25 mg/kg to 1 g orally 8 hourly for 7 d + clarithromycin 7.5 mg/kg to 250 mg orally 12 hourly for 7 d or roxithromycin 4 mg/kg to 150 mg orally 12 hourly for 7 d

More Serious:

Tropical Australia with Diabetes, Cystic Fibrosis, Congenital Heart Disease: meropenem 25 mg/kg to 1 g i.v. 8 hourly + clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly for 7 d or roxithromycin 4 mg/kg to 150 mg orally 12 hourly for 5 d

Others: benyzlpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly for 7 d [if hospitalisation difficult, procaine penicillin (3 - < 6 kg: 250 mg; 6 - < 10 kg: 375 mg; 10 - < 15 kg: 500 mg; 15 - < 20 kg: 750 mg) i.m. daily for 5 d] + clarithromycin 12.5 mg/kg to 500 mg orally for 7 d or roxithromycin 4 mg/kg to 150 mg orally 12 hourly for 5 d

Adult: calculate PSI score: to patient age in years (male) or patient age in years - 10 (female), add (for each listed condition): 30 if neoplastic disease, arterial pH < 7.35; 20 if liver disease, acutely altered mental state, respiratory rate ≥ 30/min, systolic blood pressure < 90 mm Hg, serum urea ≥ 11 mmol/L, serum sodium < 130 mmol/L; 15 if temperature < 35°C or ≥ 40°C; 10 if nursing home patient, congestive cardiac failure, cerebrovascular disease, chronic renal disease, pulse rate ≥ 125/min, serum glucose ≥ 14 mmol/L, hematocrit < 30%, pO_2 < 60 mmHg or O_2 ≤ 90% saturation, pleural effusion on chest X-ray

PSI Score ≤ 70: 30 d mortality 0.1-0.6%; treat as outpatient with amoxycillin 1 g orally 8 hourly for 7 d (procaine penicillin 1.5 g i.m. daily if oral therapy unsuitable) + doxycycline 200 mg orally first dose then 100 mg daily for further 5 d or roxithromycin 300 mg orally daily for 5 d

Non-immediate Penicillin Hypersensitivity: replace amoxycillin with cefuroxime 500 mg orally 12 hourly for 7 d

Immediate Penicillin Hypersensitivity: moxifloxacin 400 mg orally daily for 7 d as single drug

PSI Score 71-130: 30 d mortality 0.9-9.3%; treat in ward or as hospital in home

Tropical Australia with Diabetes, Alcoholism, Chronic Renal Failure or Chronic Lung Disease: gentamicin 4-6 mg/kg i.v. daily + ceftriaxone 2 g i.v. daily

Others: benzylpenicillin 1.2 g i.v. 6 hourly or amoxy(ampi)cillin 1 g i.v. 6 hourly until significant improvement then amoxycillin 1 g orally 8 hourly for total 7 d + doxycycline 100 mg orally daily for further 7 d or clarithromycin 500 mg orally 12 hourly for 7 d or roxithromycin 300 mg orally daily for 5 d

Non-immediate Penicillin Hypersensitivity: replace penicillin with ceftriaxone 1 g i.v. daily or cefotaxime 1 g i.v. 8 hourly until significant improvement then cefuroxime 500 mg orally 12 hourly for total 7 d

Immediate Penicillin Hypersensitivity: moxifloxacin 400 mg orally daily for 7 d

PSI Score > 130: 30 d mortality 27%; consider ICU admission

Non-tropical Regions: azithromycin 500 mg i.v. daily or erythromycin 0.5-1 g i.v. 6 hourly (preferably through central line) + ceftriaxone 1 g i.v. daily or cefotaxime 1 g i.v. 8 hourly or [benzylpenicillin 1.2 g i.v. 4 hourly + gentamicin 4-6 mg/kg i.v. daily (adjust dose for renal function)]

Immediate Penicillin Hypersensitivity: azithromycin or erythromycin + moxifloxacin 400 mg i.v. daily

Tropical Australia With Diabetes, Alcoholism, Chronic Renal Failure or Chronic Lung Disease: meropenem 25 mg/kg to 1 g i.v. 8 hourly or imipenem 25 mg/kg to I g i.v. 6 hourly + azithromycin 500 mg i.v. daily or erythromycin 500 mg to 1 g i.v. 6 hourly (preferably through central line)

Aspiration Pneumonia: benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly + metronidazole 12.5 mg/kg to 500 mg i.v. or 10 mg/kg to 400 mg orally 12 hourly till significant improvement then amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly

Immediate Penicillin Hypersensitivity: clindamycin 10 mg/kg to 450 mg i.v. or orally 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly till significant improvement then clindamycin 10 mg/kg to 450 mg orally 8 hourly

Gram Negative Suspected (e.g, Alcoholic): metronidazole 12.5 mg/kg to 500 mg i.v. or 10 mg/kg to 400 mg orally 12 hourly + ceftriaxone 25 mg/kg to 1 g i.v. daily or cefotaxime 25 mg/kg to 1 g i.v. 8 hourly; piperacillin-tazobactam 100/12.5 mg/kg to 4/0.5 g i.v. 8 hourly or ticarcillin-clavulanate 50/1.7 mg/kg to 3/0.1 g i.v. 6 hourly as single agent

Hospital-acquired

Low Risk of Multidrug Resistant Organisms:

Mild: amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for 7 d or if unable to take oral therapy benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly + gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function)

Penicillin Hypersensitive (Not Immediate) or Creatinine Clearance < 20 mL/min): cefuroxime 10 mg/kg to 500 mg orally 12 hourly for 7 d

Immediate Penicillin Hypersensitivity: moxifloxacin 400 mg orally daily for 7 d (adults only)

Moderate or Severe: ceftriaxone 25 mg/kg to 1 g i.v. daily, cefotaxime 25 mg/kg to 1 g i.v. 8 hourly, ticarcillin-clavulanate 50 + 1.7 mg/kg to 3 + 0.1 g i.v. 6 hourly, benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly + gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) daily (adjust dose for renal function)

Immediate Penicillin Hypersensitivity: moxifloxacin 400 mg orally or i.v. daily for 7 d (adults only)

Diabetes, Coma, Renal Failure or Head Injury: di(flu)cloxacillin 50 mg/kg to 2g i.v. 6 hourly + gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. daily

MRSA Proven: vancomycin 20 mg/kg to 1 g i.v. 12 hourly

High Risk of Multidrug Ressitant Organisms: gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. daily + piperacillin-tazobactam 100/12.5 mg/kg to 4/0.5 g i.v. 8 hourly or ticarcillin-clavulanate 50/1.7 mg/kg to 3/0.1 g i.v. 6 hourly or (if penicillin hypersensitive) cefepime 50 mg/kg to 2 g i.v. 12 hourly; if high prevalence of MRSA, add vancomycin 20 mg/kg to 1 g i.v. 12 hourly; if

indicated by susceptibility testing, imipenem 25 mg/kg to 1 g i.v. 6 hourly or meropenem 25 mg/kg to 1 g i.v. 8 hourly; if immunosuppressed, on high-dose steroids, diabetic, with malignancy or end-stage renal failure, history of smoking or excessive alcohol usage, or known local prevalence of hospital-acquired *Legionella*, add erythromycin 10 mg/kg to 0.5-1 g i.v. 6 hourly or ciprofloxacin 10 mg/kg to 400 mg i.v. or 500-750 mg orally 12 hourly

Streptococcus pneumoniae: broad spectrum cephalosporin + vancomycin until sensitivities available

Penicillin MIC < 2 mg/L: benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly until significant improvement, then amoxycillin 25 mg/kg to 1 g orally 8 hourly for total 7 d

Penicillin Hypersensitive (Not Immediate): ceftriaxone 25 mg/kg to 1 g i.v. daily until significant improvement, then cefuroxime 10 mg/kg to 500 mg orally 12 hourly for total 7 d

Immediate Penicillin Hypersensitivity: moxifloxacin 400 mg orally or i.v. daily for 7 d

Penicillin MIC ≥ 2 mg/L: vancomycin

Other Streptococci, *Neisseria meningitidis*: penicillin, erythromycin; drainage of purulent material from pleural space

Haemophilus influenzae: amoxycillin 25 mg/kg to 1 g orally 8 hourly for 7-14 d, benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly for 7-14 d, amoxycillin-clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 12 hourly for 7-14 d, cefotaxime 25 mg/kg to 1 g i.v. 8 hourly for 7-14 d, ceftriaxone 25 mg/kg to 1 g i.v. daily for 7-14 d, cefuroxime 10 mg/kg to 500 mg orally 12 hourly for 7-14 d, doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 7-14 d (not < 8 y)

Staphylococcus aureus: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly for 4-6 w, cephalothin 50 mg/kg to 2 g i.v. 6 hourly for 4-6 w, cephazolin 50 mg/kg to 2 g i.v. 8 hourly for 4-6 w; substitute vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. over 60 min 12 hourly (monitor blood levels and adjust dose accordingly) for 4-6 w if methicillin resistant suspected or proven or if severe penicillin hypersensitivity

***Staphylococcus aureus* Enterotoxin B:** supplemental oxygen, hydration, pain relievers

***Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Chlamydophila psittaci*:** doxycycline 200 mg orally first dose then 100 mg orally daily for 14 d (not in pregnant or children < 14 y), clarithromycin 7.5 mg/kg to 250 mg orally 12 hourly for 14 d, roxithromycin 300 mg orally daily (child: 4 mg/kg to 150 mg orally 12 hourly) for 4 d

***Moraxella catarrhalis*:** amoxycillin-clavulanate 500/125 mg orally 8 hourly (< 40 kg: 40/10 mg/kg/d in 3 equally divided doses) for 7-10 d, erythromycin 500 mg i.v. 6 hourly (child: 50 mg/kg/d to maximum 2 g/d i.v. in divided doses) for 10 d

Anaerobes:

Mild: amoxycillin-clavulanate 500/125 mg orally 8 hourly (child: 40/10 mg/kg/d to maximum 1.5/0.375 g/d in 3 equally divided doses) for 7-10 d; ampicillin-sulbactam

Moderate to Severe: benzylpenicillin 1.2 g i.v. 4 hourly (neonates: 60 mg/kg/d in 3 or 4 divided doses; child < 45 kg: 150 mg/kg/d in 6 divided doses) for 10-14 d ± metronidazole 500 mg i.v. infused over 20 min 8 hourly for 1-2 d then 200-400 mg orally 8 hourly or 0.5-1 g rectally 8 hourly for 10-14 d; clindamycin 600 mg i.v. diluted in 100 mL and infused over at least 30 min 8 hourly (child: 15-25 mg/kg/d to maximum 1.8 g i.v. in 3 or 4 divided doses) then 150-300 mg orally 6 hourly

***Legionella pneumophila*:** azithromycin 500 mg i.v. or orally daily or doxycycline 100 mg i.v. or orally 12 hourly or erythromycin 7.5 mg/kg to 500 mg to 1 g i.v. (preferably through central line) 6 hourly or 500 mg orally 6 hourly or erythromycin ethyl succinate 800 mg orally 6 hourly + (very severe cases requiring ICU) ciprofloxacin 400 mg i.v. or 750 mg orally 12 hourly or rifampicin 7.5 mg/kg to 600 mg i.v. or orally daily for 7-14 d if immunocmpetent or 14-21 d if immunocompromised

Chromobacterium violaceum: chloramphenicol

***Francisella tularensis*:** streptomycin or gentamicin for 10 d

***Vibrio vulnificus*:** doxycycline 100 mg orally or i.v. twice daily + ceftazidime 2 g i.v. 3 times a day or ciprofloxacin 400 mg twice a day for 3 d or gentamicin

Pseudomonas aeruginosa: gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose dor renal function) + piperacillin 50-75 mg/kg to 3-4 g i.v. 6 hourly or cefepime 50 mg/kg to 2 g i.v. 12 hourly or ceftazidime 50 mg/kg to 2 g i.v. 8 hourly or ciprofloxacin 10 mg/kg to 400 mg i.v. or 15 mg/kg to 750 mg orally 12 hourly for 14-21 d

Burkholderia cepacia: imipenem

Burkholderia pseudomallei: cotrimoxazole + ceftazidime or meropenem or imipenem

***Stenotrophomonas maltophilia*:** cotrimoxazole

Enterobacter, Serratia: gentamicin 5 mg/kg i.v. daily (child: 7.5 mg/kg/d i.v. in 1-3 divided doses) + meropenem 10 mg/kg to 500 mg i.v. 8 hourly or ciproflxacin 5 mg/kg to 200 mg i.v. 8 hourly for 7-14 d

Acinetobacter baumannii: meropenem 25 mg/kg to 1 g i.v. 8 hourly; colistin

Other Aerobic Gram Negative Bacilli (Including *Klebsiella pneumoniae*): cefotaxime 25 mg/kg to 1 g i.v. 8 hourly for 7-14 d, ceftriaxone 25 mg/kg to 1 g i.v. daily for 7-14 d, gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) daily (adjust dose for renal function) for 7-14 d, piperacillin-tazobactam 100 + 12.5 mg to 4 + 0.5 g i.v. 8 hourly for 7-14 d, ticarcillin + clavulanate 50 + 1.7 mg/kg to 3 + 0.1 g i.v. 6 hourly for 7-14 d, ciprofloxacin 10 mg/kg to 400 mg i.v. or 15 mg/kg to 750 mg orally 12 hourly for 7-14 d, meropenem 12.5 mg/kg to 500 mg i.v. 8 hourly for 7-14 d

***Corynebacterium pseudodiphtheriticum*:** vancomycin ± tobramycin

Rhodococcus equi: vancomycin ± imipenem for at least 3 w, then oral rifampicin + macrolide or tetracycline for at least 2 mo

Anthrax: ciprofloxacin 10 mg/kg to 400 mg i.v. every 12 h or doxycycline 2.5 mg/kg to 100 mg i.v. every 12 h (not < 8 y) + rifampicin, vancomycin, benzylpenicillin, clindamycin, chloramphenicol, imipenem, amoxy/ampicillin or clarithromycin for 14-21 d then ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly or doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not < 8 y) or amoxycillin 15 mg/kg to 500 mg orally 8 hourly for total 60 d

Plague: gentamicin 4-7.5 mg/kg i.v. daily, doxycycline 5 mg/kg to 200 mg i.v. then 2.5 mg/kg to 100 mg i.v. twice daily (not < 8 y), ciprofloxacin 15 mg/kg to 400 mg i.v. twice daily, chloramphenicol 25 mg/kg i.v. 4 times a day

Lactobacillus: vancomycin i.v. for 14 d

Influenza A: amantidine or rimantidine

Adenovirus: ribavirin i.v. loading dose 30 mg/kg/d then 15 mg/kg/d in divided doses every 6 h

Pneumocystis jiroveci:

Mild to Moderate (PaO_2 > 70 mm Hg, Alveolar-Arterial Gradient > 35 mm Hg, Oxygen Saturation > 94%): cotrimoxazole 5 + 25 mg/kg to 7 + 35 mg/kg orally 8 hourly for 21 d or (if sulphamethoxazole contraindicated) dapsone 1-2 mg/kg to 100 mg orally daily + trimethoprim 5 mg/kg to 300 mg orally 8 hourly for 21 d or (if hypersensitive to cotrimoxazole) atovaquone 750 mg orally 12 hourly for 21 d

Severe: cotrimoxazole 5 + 25 mg/kg orally or i.v. 6 hourly for 21 d or pentamidine 4 mg/kg to 300 mg i.v. daily for 21 d if unresponsive + prednis(ol)one 1 mg/kg to 40 mg orally 12 hourly for 5 d then daily for 5 d then 0.5 mg/kg to 20 mg daily for 11 d in HIV

***Paragonimus*:** praziquantel, bithionol

Prophylaxis:

***Streptococcus pneumoniae*:** 23-valent polysaccharide vaccine 80% efficacy; fever 4%, severe systemic reaction 0.01%, risk of Arthus reaction with second dose; duration of immunity 3-8 y, cost-benefit ratio 0.13-0.77 for all adults, 0.38-2.32 for high risk adults (those with cardiovascular disease and chronic pulmonary disease entailing increased morbidity from respiratory infections, alcoholism, cirrhosis of liver, CSF leaks, HIV infection, lymphoma, leukemia, diabetes mellitus, Hodgkin's disease, immunosuppression, multiple myeloma, generalised malignancy, chronic renal failure, postrenal transplant, postsplenectomy, skull fractures with recurrent pneumococcal meningitis, splenic dysfunction, otherwise healthy adult ≥ 65 y); also consider for children ≥ 2 y with anatomic splenectomy or functional asplenia associated with sickle cells, CSF leaks, immunosuppression, nephrotoxic syndrome, splenectomy

***Haemophilus influenzae* type b:** given to index case before discharge, and within 7 d to all household contacts of index case, including incompletely immunised children < 4 y and any immunocmpromsed child; also adults and children at day care centres with 2 or more cases of invasive disease in 60 d period and with incompletely immunised children; rifampicin 20 mg/kg to maximum 600 mg (child < 1 mo: 10 mg/kg) orally daily for 4 d (not pregnant; give ceftriaxone 1 g in lignocaine hydrochloride 1% i.m. as single dose); vaccine to index case under 2 y even if previous immunisation and to unvaccinated contacts < 5 y; all children should be

routinely vaccinated beginning at 2 mo (95-100% efficacy; swelling, redness and pain at injection site in 5-30%, fever and irritability uncommon, serious reactions rare; contraindicated if anaphylaxis to vaccine components or previous dose and serious illnesses)

Neisseria meningitidis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

Ventilator-associated Pneumonia: chest physiotherapy

Anthrax (Post-exposure): doxycycline 2.5 mg/kg to 100 mg orally twice daily for 60 d (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally twice daily for 60 d, amoxycillin 15 mg/kg to 500 mg orally 3 times daily for 60 d; consider 3 doses of anthrax vaccine 0, 2 and 4 w after exposure

Tularemia (Post-exposure): doxycycline 2 mg/kg to 100 mg orally 12 hourly for 14 d

Plague (Postexposure): doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly

Asplenic and Postsplenectomy: pneumococcal, meningococcal, Hib and standard schedule immunisation (including annual influenza); antibiotic prophylaxis in asplenic children < 5 y, children < 5 y with sickle cell anaemia, for at least 2 y following splenectomy and patients with severe underlying immunosuppression: amoxycillin 125 mg orally 12 hourly (< 2 y: 20 mg/kg orally daily) or phenoxymethylpenicillin 250 mg (< 2 y: 125 mg) orally 12 hourly or if penicillin hypersensitive roxithromycin 4 mg/kg to 150 mg orally daily or erythromycin 250 mg orally daily or erthryomycin ethyl succinate 400 mg orally daily

Cirrhotic Patient with Gastrointestinal Bleeding: norfloxacin 400 mg orally commencing 1 h before endsocopy and then 12 hourly for 1-2 d or if oral therapy not feasible ciprofloxacin 400 mg i.v. at time of induction and then 12 hourly for 1-2 d

NECROTISING PNEUMONIA: extensive destruction of lung tissue resulting in formation of multiple small abscess cavities; often fatal

Agents: *Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus mirabilis,* other Enterobacteriaceae, anaerobes, Panton-Valentine leukocidin positive strains of *Staphylococcus aureus* (young patients)

Diagnosis: culture of lung aspirate

Treatment: broad spectrum penicillin + aminoglycoside

CYSTIC FIBROSIS (MUCOVISCOIDOSIS): patients often suffer from chronic bacterial pulmonary infection

Organisms: *Pseudomonas aeruginosa* in 30-40% of patients (colonisation to severe necrotising bronchopneumonia; mucoid strains in chronic infection), *Burkholderia cepacia* in 10-40% (associated with accelerated lung disease, sepsis and necrotising pneumonia), *Haemophilus influenzae* and *Staphylococcus aureus* common; also, *Stenotrophomonas maltophilia, Pseudomonas alcaligenes, Achromobacter xylosoxidans, Acinetobacter baumanii, Ralstonia, Pandoraea, Mycobacterium abscessus,* fungi and yeasts

Diagnosis: sputum culture

Treatment:

Haemophilus influenzae: amoxycillin-clavulanate 500/125 mg orally 8 hourly (< 40 kg: 40/10 mg/kg orally daily in divided doses) + probenecid 500 mg orally 6 hourly (child: 10-15 mg/kg orally daily in divided doses); in penicillin allergy: erythromycin 500 mg orally 6 hourly (child: 50 mg/kg orally daily in divided doses) ± rifampicin 600-1200 mg (child: 15-20 mg/kg) orally daily in divided doses, or cotrimoxazole 160/800 mg (6 w - 5 mo: 20/100 mg; 6 mo - 5 y: 40/200 mg; 6-12 y: 80/400 mg) orally 12 hourly; ceftazidime 150 mg/kg to maximum 6 g i.v. daily in divided doses for 2 weeks; aztreonam (1 w - 2 y: 30 mg/kg; > 2 y: 50 mg/kg) i.v. 6 hourly ± amikacin 1.5 mg/kg i.v. daily in 2 or 3 divided doses

***Pseudomonas aeruginosa*:**

First Isolate: colistin 1 MU inhaled twice daily + oral ciprofloxacin for 3 w

Second Isolate: colistin 2 MU inhaled 3 times daily + oral ciprofloxacin for 3 w

Third Isolate Within 6 mo: colistin 2 MU inhaled 3 times daily + oral ciprofloxacin for 3 mo

Chronic Infection: chronic suppressive inhalation therapy with colistin 1 MU twice daily or tobramycin 80 mg twice daily, alternated monthly

Acute Exacerbation:

First Line: ciprofloxacin

Second Line: ticarcillin 200-300 mg/kg i.v. daily in 4-6 equally divided doses or piperacillin 100-300 mg/kg/d to 16 g i.v. in 3 divided doses + tobramycin (pediatric: 6-7.5 mg/kg/d i.v. in 3-4 divided doses daily; adults: 8-10 mg/kg/d i.v. in 3-4 divided doses daily)

Third Line: piperacillin-tazobactam or ticarcillin-clavulanate + tobramcyin

Fourth Line or Penicillin Hypersensitive: ceftazidime 100-150 mg/kg/d to 2 g (paediatric) or 3 g (adult) 3 times daily + tobramycin

Fifth Line: aztreonam + tobramycin

Sixth Line: imipenem or meropenem 25-40 mg/kg to 2 g i.v. 8 hourly

Seventh Line: high dose ceftazidime + tobramycin + oral chloramphenicol or trimethoprim or doxycycline

clarithromycin and azithormycin lead to improvement in respiratory function through inhibition of alginate production by mucoid strains; possible benefit of piroxicam (NSAID)

Burkholderia cepacia: tobramycin aerosol + i.v. meropenem + i.v. ceftazidime, chloramphenicol, cotrimoxazole or aztreonam; amiloride aerosol + tobramycin aerosol

Stenotrophomonas maltophilia: cotrimoxazole, doxycycline, timentin

Achromobacter xylosoxidans: colistin, minocycline, imipenem, meropenem, piperacillin, piperacillin-tazobactam

Acinetobacter baumanii: polymyxin B, sulbactam

***Staphylococcus aureus*:** cloxacillin/flucloxacillin 2 g i.v. 4 hourly (< 2 y: ¼ dose; 2-10 years: ½ dose) + fusidic acid 500 mg orally 8 hourly (child: 50 mg/kg orally daily in divided doses) + probenecid 500 mg orally 6 hourly (child: 10-15 mg/kg orally daily in divided doses) for 14 d; in persistent infection, methicillin 500 mg by inhalation 12 hourly may be added; in penicillin allergy, use rifampicin 500 mg orally 12 hourly (child: 15 mg/kg orally daily in divided doses) + fusidic acid

Mycobacterium abscessus: dependent on susceptibility tests

Prophylaxis: *Haemophilus influenzae* type b conjugate vaccine (diphtheria toxoid conjugate) at 18 mo or older

NEONATAL PNEUMONIA

Agents: *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Streptococcus agalactiae* (early onset; 75% mortality), *Ureaplasma urealyticum, Simplexvirus* (onset days 3-14)

Diagnosis: chest X-ray; Gram stain and culture of gastric aspirate, pleural fluid or lung aspirate

Staphylococcus aureus: alveolar disease, consolidation, presence of air bronchograms and pleural effusions on X-ray

Herpes: prominent hila with central interstitial infiltrate on X-ray; thrombocytopenia, evidence of disseminated intravascular coagulation, elevated liver function tests, lymphoid pleocytosis in CSF; vesicular skin lesions may be present; antigen tests and culture

Treatment:

Ureaplasma urealyticum: erythromycin

Other Bacteria: benzylpenicillin 60-120 mg/kg/d i.v. in 4-6 divided doses for 7-10 d + cloxacillin

Herpes: aciclovir

PRIMARY PNEUMONIA IN INFANTS (EOSINOPHILIC PERTUSSOID SYNDROME OF INFANCY): interstitial pneumonia affecting 1-2% of infants aged 1-4 mo (50% with conjunctivitis); transmitted from infected mothers during parturition; similar symptoms in AIDS

Agent: *Chlamydia trachomatis*; note that *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus* may also cause pneumonia in infants

Diagnosis: no or low grade fever, no rigours, somewhat pertussis-like staccato paroxysmal cough with wheezing but without an inspiratory whoop; no bacteria on Gram stain of sputum; absolute increase in eosinophils in blood smear; diffuse interstitial infiltrates and hyperinflation, peribronchial thickening and scattered areas of atelectasis on X-ray; immunofluorescence; serology (complement fixation test; IgM or high sustained IgG)

Treatment: erythromycin base or ethylsuccinate 50 mg/kg/d orally in 4 divided doses for 14 d

TUBERCULOUS PNEUMONIA: occurs especially in impaired cell-mediated immunity and in 4% of tuberculous patients with underlying neoplasia (100% mortality in these cases)

Agent: *Mycobacterium tuberculosis*

Diagnosis: remittent or intermittent fever of 38-38.5°C, rigours rare, cough variable, usually productive; white cell count < 10,000/μL; seen in children and the elderly; may be rapidly progressive; exposure to known tuberculosis source; upper lobe infiltrate; Ziehl-Neelsen stain and mycobacterial culture of sputum; PCR (sensitivity 90%, specificity 99.6%)
Treatment: rifampicin 10 mg/kg to 600 mg orally 1 h before breakfast daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo + isoniazid 10 mg/kg to 300 mg orally daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby: 5 mg) with each dose] + ethambutol 15 mg/kg orally daily or 30 mg/kg orally 3 times weekly (not < 6 y) for 2 mo or until known to be susceptible to rifampicin and isoniazid (to 6 mo) + pyrazinamide 25 mg/kg to 2 g orally 8 daily or 50 mg/kg to 3 g orally 3 times a week for 2 mo or 6 mo if not known to be suceptible to rifampicin and isoniazid
Prophylaxis: isoniazid 10 mg/kg to 300 mg orally daily for 6-9 mo in recent tuberculin converters, children with positive tuberculin reactions, persons with inactive tuberculosis who are immunosuppressed (HIV, long-term corticosteroids, immunosuppressive or cytotoxic drugs, radiotherapy)

Diffuse Interstitial Pneumonia

Agents: 36% *Pneumocystis jiroveci* (occurs in 85% of AIDS patients; associated with corticosteroids in 77% of non-AIDS patients; also in other adults with an impaired immune response, especially chemotherapeutically immunosuppressed, T cell deficiency; also plasma cell pneumonia in newborn infants); Gram negative enteric and non-fermentative aerobic bacilli (in granulocytopenia), *Streptococcus pyogenes, Staphylococcus aureus* (in granulocytopenia), *Nocardia asteroides* (in T cell deficiency), *Mycobacterium* (in T cell deficiency; *M.avium-intracellulare* hot tub lung in immunocompetent), *Rhodococcus equi* (in immunocompromised patients), *Aspergillus* (in granulocytopenia), *Mucor* (in granulocytopenia), *Absidia, Rhizopus, Candida, Cryptococcus neoformans* (in T cell deficiency and AIDS), *Histoplasma capsulatum, Coccidioides immitis, human human cytomegalovirus* (≈ 50% of cases in allogenic bone marrow transplant recipients), *human herpesvirus 3*, *Simplexvirus* (in T cell deficiency), *Strongyloides stercoralis, Toxoplasma gondii,* ? *Mycoplasma*, ? *Ureaplasma*; 27% due to underlying disease (particularly lymphomas, sarcoidosis); also due to radiation and chemotherapeutic agents
Diagnosis: history as to underlying disease, radiation therapy and pulmonary toxic medications; Gram-Weigert, Gram, Ziehl-Neelsen, Giemsa, methenamine-silver and toluidine blue O stains and KOH preparation of induced sputum and bronchoalveolar lavage (sensitivity 89%; Ringer's solution most suitable; can be performed despite bleeding tendencies but yield may not be as good as from biopsy; complications rare; contraindicated in severe hypoxemia), transtracheal aspiration (useful initial step in evaluation that bypasses oropharyngeal contamination; occasional bleeding), open biopsy (requires general anaesthesia; because of large sample obtained, gives highest yield; < 10% delayed pneumothorax), transbronchial biopsy (low morbidity, but limited sample; results superior to simultaneous brushing; 10% pneumothorax incidence), transtracheal bronchial brushing (limited sample; may be attempted after platelet transfusion; some complication in almost 20% of patients), percutaneous needle aspiration (reliable in diagnosing pneumocystosis in leukemic children, most of whom are in remission; limited sample; pneumothorax in 25% of patients), percutaneous trephine biopsy (limited sample; bleeding may be difficult to control; pneumothorax in up to 66% of attempts), fibreoptic bronchoscopy (relatively well tolerated but oropharyngeal contamination confuses results; occasional bleeding and pneumothorax if brushing also performed), or cutting needle biopsy (for more peripheral solid lesions rather than diffuse disease; complications greater in diffuse disease); blood culture; antibody serology for *human human cytomegalovirus*, *Aspergillus*, *Toxoplasma*, *influenza virus, parainfluenza virus, adenovirus, human herpesvirus 3*, *Simplexvirus*, *Mycoplasma*, *Pneumocystis jiroveci* (indirect fluorescent antibody test; restricted availability; suggests the diagnosis if positive but gives many false negatives and should not be relied on clinically), *Legionella*; cryptococcal antigen determination on serum; H&E and methenamine-silver stains of lung biopsy sections

Pneumocystis jiroveci: severe dyspnea on exertion, low grade fever, non-productive cough, malaise and cyanosis; usually in patients with CD4 counts < 200 cells/μL; chest X-ray shows diffuse bilateral interstitial infiltrates; gallium scan shows diffuse bilateral pulmonary disease; in immunompromised, pneumonic exudate contains lymphocytes, macrophages and possibly eosinophils but not polymorphs; arterial blood gas analysis shows arterial pO_2 of < 70 mm Hg or low respiratory diffusing capacity (< 80% of predicted value) or an increase in alveolar-arterial O_2 gradient; Wright-Giemsa, Papanicolaou, methenamine silver staining, direct immunofluorescence of induced sputum (sensitivity 30-90%), bronchoalveolar lavage (sensitivity 98-100%), brush biopsy of bronchus or needle biopsy of lung (sensitivity 90-95%); counterimmunoelectrophoresis; indirect fluorescent antibody titre

Treatment:

***Pneumocystis jiroveci*:**

Mild to Moderate: cotrimoxazole 5/25 mg/kg to 320/1600 mg orally 8 hourly for 3 w; if cotrimoxazole undesirable, trimethoprim 5-7.5 mg/kg to 300 mg orally 12 hourly for 3 w + dapsone 1-2 mg/kg to 100 mg orally daily for 3 w; atovaquone 750 mg orally twice daily with meals for 21 d

Severe: cotrimoxazole 5/25 mg/kg to 320/1600 mg i.v. 6 hourly until improvement occurs, then oral cotrimoxazole as above; if no response to, or intolerant of, cotrimoxazole, consider desensitisation or use pentamidine isethionate 4 mg/kg daily to 300 mg by i.v. infusion over 1-2 h for 3 w or 600 mg in 6 mL of water as an aerosol 20 min daily for 21 d; eflornithine 400 mg/kg daily i.v. in 4 divided doses for 10 days, then 300 mg/kg daily in 4 divided doses for 4 d, then 300 mg/kg daily orally thereafter; trimetrexate 30 mg/m^2 of body surface as i.v. bolus daily for 21 d + calcium folinate (leucovorin) 20 mg/m^2 of body surface as i.v. bolus 6 hourly for 23 d + sulphadiazine 1 g orally 6 hourly for 6 d; clindamycin 600 mg i.v. 6 hourly for 3 w or 600 mg i.v. as a loading dose followed by 300-450 mg orally 6 hourly for 3 w + primaquine 15 mg base orally once daily for 3 weeks; if significant hypoxia (especially in HIV), prednisolone 1 mg/kg to 40 mg orally or i.v. for 5 d, then 1 mg/kg to 40 mg daily for 5 d, then 0.5 mg/kg to 20 mg daily for 11 d

Maintenance Therapy and Primary Prophylaxis in HIV/AIDS (CD4 Count < 200/μL): cotrimoxazole 80/400 or 160/800 mg orally daily or 160/800 mg orally 3 times weekly, dapsone 100 mg orally 3 times weekly, pentamidine 300 mg i.v. or aerosolised every 2-4 w

Bacterial: depending on specific agent (*Rhodococcus equi*: rifampicin + erythromycin)

Cryptococcus neoformans:

Mild: fluconazole 20 mg/kg to 800 mg orally or i.v. initially, then 10 mg/kg to 400 mg orally daily for at least 4 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2 w; if clinical improvement after 2 w, change to fluconazole as for **Mild**

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

Other Fungal:

Non-neutropenic with Milder Disease: voriconazole 200 mg orally 12 hourly, itraconazole 7.5 mg/kg to 300 mg orally 12 hourly for 3 d then 5 mg/kg to 200 mg 12 hourly

Immunocompromised: voriconazole 6 mg/kg i.v. 12 hourly for 2 doses then 4 mg/kg 12 hourly for at least 7 d then 4 mg/kg to 200 mg orally 12 hourly, amphotericin B desoxycholate 1 mg/kg i.v. daily

Simplexvirus: famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

Human herpesvirus 3: famciclovir 500 mg orally 8 hourly for 7-14 d, valaciclovir 1 g orally 8 hourly for 7-14 d, aciclovir 800 mg orally 5 times daily for 7-14 d

Severe or Unable to Take Oral Therapy: aciclovir 10 mg/kg i.v. 8 hourly for 7-14 d (adjust dose for renal function)

Human human cytomegalovirus: valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly (adjust dose according to creatinine clearance), cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid; not if proteinuria > 2+ or creatinine clearance < 55 mL/min) then as above every 2 w

Other Viral: non-specific

Toxoplasma gondii: sulphadiazine 1-1.5 g orally or i.v. 6 hourly for 3-6 w then 500 mg orally 6 hourly or 1 g orally 12 hourly + pyrimethamine 50-100 mg orally loading dose then 25-50 mg daily for 3-6 w (continue if necessary)

Sulphadiazine Hypersensitive: substitute clindamycin 600 mg orally or i.v. 6 hourly for 3-6 w (treatment) or 600 mg orally 8 hourly (maintenance) for sulphadiazine

Strongyloides stercoralis: thiabendazole

Prophylaxis:

***Pneumocystis jiroveci* in AIDS Patients with Rapid Fall in Number of $CD4^+$ Cells, $CD4^+$ 20-30%, $CD4^+$ Total Count < 200/µL, Fever or Thrush, or to Prevent Recurrence of Infection:** cotrimoxazole 80/400-160/800 mg orally once daily or 160/800 mg orally twice daily on 3 days of week or 12 hourly twice weekly; dapsone 100 mg orally 3 times a week; pentamidine isethionate 300 mg i.v. or in 6 mL of water as a 20 minute aerosol from nebuliser producing droplet size ≤ 2 µm every 2-4 w; clindamycin + primaquine; atovaquone 1500 mg daily; pyrimethamine + sulphadiazine; dapsone 100 mg orally twice a week + trimethoprim 300 mg orally twice a week; pyrimethamine-sulphadoxine (Fansidar) 25/500 mg orally weekly; immunologic monitoring; zidovudine

Human human cytomegalovirus: exclusive use of *human human cytomegalovirus*-seronegative blood products; gangiclovir 5 mg/kg i.v. every 12 h for 5-7 d, then 5-6 mg/kg i.v. daily for 5 d/w from engraftment until day 100 after haematopoietic stem cell transplantation

Toxoplasma gondii: cotrimoxazole 1 double strength tablet orally daily or 1 single strength tablet orally daily or 1 double strength tablet orally 3 times/w to seropositive allogenic adult or adolescent hematopoietic stem cell transplant recipients as long as on immunosuppressive therapy and to HIV/AIDS patients with CD4 count < 200/µL

Giant Cell Pneumonia Error! Bookmark not defined.

Agent: measles virus; occurs in 4-75% of measles cases, causing 75% of measles deaths overall and 100% of deaths in patients < 5 y

Diagnosis: patchy consolidation at bases of lungs; viral culture and cytology of throat swab; serology (complement fixation test, hemagglutination inhibiton)

Treatment: non-specific

Fungal Pneumonia: usually in immunosuppressed patients (aspergillosis, zygomycosis and cadidiasis especially in neutropenics; aspergillosis in 4% of bone marrow transplant recipients; cryptococcosis, ? histoplasmosis especially in impaired cell-mediated immunity; coccidioidomycosis (8% of symptomatic infections) risk factors diabetes, smoking, older age,) but may occur in general population (32% of *Aspergillus* isolates from sputum and 66% from bronchial washings are associated with pulmonary infiltration; 40-45% of these cases are in non-immunocompromised patients, 20-40% of whom have invasive pulmonary aspergillosis); necrotising bronchopneumonia in 35% of patients with pulmonary aspergillosis, hemorrhagic infarction in 30%, miliary microabscesses in 10%, lobar pneumonia in 10%, bronchitis in 10%, focal abscesses in 5%, solitary abscess in 5%

Agents: isolates of *Blastomyces dermatitidis, Coccidioides immitis, Histoplasma capsulatum* and *Sporothrix schenckii* are always significant; isolates of *Absidia, Aspergillus (Aspergillus fumigatus, Aspergillus flavus,* occasionally other *Aspergillus* species; most common cause of community acquired pneumonia (often with concurrent gram negative bacilli) in stem cell transplant recipients with graft versus host disease), *Candida*, *Cryptococcus neoformans*, *Mucor*, *Rhizopus* and *Rhizomucor* may be significant, especially in leukemics; also *Trichosporon, Fusarium, Penicillium* and *Torulopsis* in cancer patients, and *Drechslera, Geotrichum, Pseudallescheria boydii, Scedosporium prolificans* and *Cunninghamella* in disseminated infections

Diagnosis: wet mount KOH phase contrast microscopy and fungal culture of bronchoalveolar lavage (100% sensitivity in diffuse pulmonary disease due to *Aspergillus* but not effective in patients with focal pulmonary lesions), Gomori methenamine silver sections and culture of lung biopsy; immunodiffusion; precipitin (positive in 90% of aspergilloma cases, 60-75% of allergic bronchopulmonary aspergillosis, rare in other circumstances); halo sign on CT indicative of invasive aspergillosis

Treatment:

Cryptococcus neoformans:

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

Others: amphotericin B (not *Pseudallescheria boydii*, *Scedosporium prolificans*; disseminated aspergillosis: 0.5-1 mg/kg/d i.v. to total 2-8 g; blastomycosis: 0.5-1 mg/kg/d i.v. to total 1.5-2 g; coccidioidomycosis: 1-1.5 mg/kg/d i.v. to total 1.5-2 g; histoplasmosis: 0.6 mg/kg/d i.v to total 2-2.5 g; consider

administration through a percutaneous endobronchial catheter, combined with systemic administration, if this seems necessary; may be combined with flucytosine 10-20 g/d), voriconazole 6 mg/kg i.v. 12 hourly for 2 doses then 4 mg/kg 12 hourly for at least 7 d then 4 mg/kg to 200 mg orally 12 hourly, itraconazole + flucytosine, miconazole; early surgical resection in symptomatic aspergilloma, asymptomatic aspergilloma with reasonable complication, mucormycosis with persistent cavitations after treatment, and scedesporosis; decortication desirable in extensive pleural disease; interferon-gamma in pulmonary aspergillosis in chronic granulomatous disease

TROPICAL EOSINOPHILIC PNEUMONIA (TROPICAL PULMONARY EOSINOPHILIA, FRIMODT-MOLLER SYNDROME, TROPICAL EOSINOPHILIA, TROPICAL EOSINOPHILIC ASTHMA, TROPICAL EOSINOPHILOSIS, WEINGARTEN DISEASE, WEINGARTEN SYNDROME)

Agents: *Wuchereria bancrofti, Brugia malayi, Brugia pahangi,* animal filaria; *Corynebacterium pseudotuberculosis* may cause similar syndrome

Diagnosis: chronic pulmonary infiltration and opacities, cough, dyspnea, asthma with nocturnal wheezing, X-ray; marked blood eosinophilia; microfilariae present in lung tissue but absent from peripheral blood; high IgE; positive filarial serology (filaria-specific IgG and IgE)

Treatment: diethylcarbamazine

PNEUMONITIS

Agents: *respiratory syncytial viru*s (6-12 mo; in 25% of cases; wheezing common), parainfluenza, influenza A and B, adenovirus, *measles virus*, varicella, *human metapneumovirus* (in 17% of cases); *Rhodococcus equi* (in immunodeficient hosts exposed to animals), *Yersinia pestis, Francisella tularensis,* anaerobes (3% mortality), *Mycoplasma pneumoniae* (in immunodeficient), *Haemophilus influenzae*, *Burkholderia pseudomallei, Mycobacterium szulgai, Mycobacterium xenopi, Nocardia asteroides,* 12% of Rocky Mountain spotted fever cases; *Cryptococcus neoformans* (chronic; can lead to fatal meningitis), *Candida albicans;* migrating larvae of *Ascaris lumbricoides,* hookworm, *Strongyloides stercoralis*; *Acanthamoeba*

Diagnosis: immunofluorescence of nasopharyngeal aspirate; viral culture of throat swab, nasopharyngeal aspirate; Gram stain and culture of sputum, bronchial washing, open lung biopsy, transtracheal aspirate; serology; observation of larvae in sputum; *Strongyloides stercoralis* gives an initial neutrophilia becoming leucopenia with 40% eosinophilia

Treatment:

Respiratory Syncytial Virus, Influenza, Parainfluenza: ribavirin aerosol

Other Viruses: non-specific

Rhodococcus equi: erythromycin + rifampicin + surgery

Francisella tularensis: streptomycin, tetracycline

Mycoplasma pneumoniae*, *Nocardia asteroides: minocycline

Haemophilus influenzae: amoxycillin-clavulanate

Anaerobes: clindamycin, metronidazole

Burkholderia pseudomallei: tetracycline 40-50 mg/kg orally daily in 4 divided doses for 60-150 d, cotrimoxazole 4/20-8/40 mg/kg (child: 6/30 mg/kg) daily orally in 2 divided doses, chloramphenicol 40-100 mg/kg (child: 50-75 mg/kg) daily orally in 4 divided doses

Mycobacterium szulgai: ethambutol 25 mg/kg to 1 g orally daily + rifampicin 600 mg daily + ethionamide 500 mg - 1 g orally daily in 3 divided doses or streptomycin 15 mg/kg i.m. daily or cycloserine 500 mg orally daily in 2 divided doses

Mycobacterium xenopi: isoniazid 300-450 mg orally daily as a single dose + rifampicin 600 mg orally daily + streptomycin 15 mg/kg i.m. daily

Cryptococcus neoformans*, *Candida albicans:

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

Larvae: pyrantel embonate, thiabendazole, mebendazole

Acute Empyema: 50% mortality in hospital-acquired cases
Agents: *Staphylococcus aureus* (25-35% in adults, 75-90% in children), anaerobes (15-35% in adults, 1% in children; *Peptostreptococcus*, *Bacteroides, Prevotella, Fusobacterium,* rare cases of *Clostridium perfringens), Streptococcus pneumoniae* (12-38% in adults, 2-5% in children), other streptococci (3-5% in adults, 2% in children; *Streptococcus pyogenes*, *Streptococcus milleri,* enterococci, *Streptococcus canis*), *Haemophilus influenzae* (0-5% in adults, 1% in children), other Gram negative bacilli (15-30% in adults, 2% in children; *Klebsiella-Enterobacter, Escherichia coli, Pseudomonas aeruginosa, Proteus, Acinetobacter calcoaceticus, Serratia marcescens*; uncommonly *Actinobacillus actinomycetemcomitans, Pseudomonas alcaligenes*; rare cases of *Capnocytophaga, Eikenella corrodens, Erwinia herbicola, Actinomyces pyogenes, Candida*; also in tuberculosis
Diagnosis: associated with pneumonia, thoracic surgery, tumour, spontaneous pneumothorax, lung or subdiaphragmatic abscess, bronchiectasis, asthma, foreign body, dental extraction, tonsillectomy; fever in 80%, dyspnea in 60%, chest pain in 50%, weight loss in 25%, chills in 25%, haemoptysis in 15%, night sweats in 12%; chest X-ray (presence of pleural effusions on an earlier film; extension of the air-fluid level to the chest wall; extension of the lesion across fissure line; a tapering border of the air-fluid pocket; location of the air pocket in the posterior costophrenic sulcus; a cavity of unequal dimensions); Gram, fungal and acid-fast stains and culture of aspirated pus from loculated empyema; total ($\geq 2500/\mu L$) and differential (polys predominate = bacterial, lymphs predominate = fungal, tuberculosis) white cell count, biochemistry (protein ≥ 3 g/dL and ratio of pleural fluid to serum content 0.5, glucose 50% that of serum, LDH ≥ 200 IU and ratio of pleural fluid to serum content 0.6, specific gravity ≤ 1.018, pH ≤ 7.2), Gram, fungal and acid-fast stains and culture of pleural fluid in nonloculated empyema
Treatment: open drainage +
Pseudomonas: ticarcillin + gentamicin
Other Bacteria: chloramphenicol
Candida: amphotericin B + flucytosine
Chronic Empyema
Agents: may be due to any of the organisms causing acute empyema, but is frequently due to, or complicated by, various fungi (mainly those causing fungal pneumonia)
Diagnosis: as for **Acute Empyema**
Treatment: surgery + appropriate antimicrobial
Pulmonary Abscess: primary in oral sepsis and decreased cough reflex (alcohol, anesthesia, drugs, seizures, neurologic disorders, coma), esophageal disorders (diverticula, achalasia, strictures, motility disorders, cancer) with oral sepsis, endobronchial obstruction (cancer, foreign body) and in postnecrotising pneumonia; opportunistic in newborn (prematurity, congenital abnormalities of the heart or lung), elderly (blood dyscrasias, cancer of the lung and oropharynx, treatment with steroids, postoperatively), and nosocomial; hematogenous in septicemia and pulmonary infarct (bland or septic)
Agents: 85-90% anaerobes (60-75% only; 50% *Fusobacterium nucleatum,* 45% *Prevotella melaninogenica,* 40% *Peptostreptococcus,* 25% *Peptococcus,* 20% *Eubacterium,* 15% *Bacteroides fragilis*, 10% *Propionibacterium*; other *Bacteroides*, other *Prevotella, Bifidobacterium adolescentis*), 23% *Staphylococcus* and *Streptococcus*, 10% *Pseudomonas aeruginosa*, 8% *Klebsiellla,* 4% *Haemophilus influenzae* (18% of non-bacteremic invasive *Haemophilus influenzae* infections in older children and adults); *Mycobacterium tuberculosis*, *Chromobacterium violaceum* (in 22% of infections due to this organism), *Rhodococcus equi*, *Capnocytophaga*, *Salmonella* (in renal transplant recipients), *Lactobacillus* (extremely rare), *Selenomonas sputigena, Legionella, Nocardia, Entamoeba histolytica* (amoebic abscess of lung or pleura is commonly secondary to an amoebic liver abscess that ruptures through the diaphragm into the lung, but may arise in the mesenteric blood vessels or lymphatics)
Diagnosis: cavitary lesion on chest X-ray (may also be due to tuberculosis, fungi including histoplasmosis, blastomycosis, coccidioidomycosis and aspergillosis, primary or metastatic carcinoma, infected cyst, infected bullae, nontuberculous granulomatous disease, extension of a subphrenic process, pulmonary infarction); culture of biopsy; fever (average minimum 38.8°C rectally) in 95%, leucocytosis (average $\approx 15{,}000/\mu L$) in 90%, anemia (average haematocrit 35%) in 90%, aspiration in 75%, weight loss (average 9 lb) in 55%
Treatment: benzylpenicillin 600 mg i.v. 4-6 hourly (child: 100-120 mg/kg/d in 4-6 divided doses) for 10-14 d + metronidazole 500 mg i.v. 12 hourly (child: 20 mg/kg/d to 1 g in 3 divided doses) for 1-2 d then 400 mg orally (child: 20 mg/kg/d to 800 mg/d in 2 divided doses) or 1 g rectally 12 hourly (child: 80 mg/kg/d to 2 g in 2 divided doses) for total 10-14 d; clindamycin 600 mg i.v. slowly 8 hourly (child: 30 mg/kg/d to 1.8 g/d in 3

divided doses), then 300 mg orally 6 hourly (child: 20-40 mg/kg/d to 1.2 g in 4 divided doses) for total 10-14 d; substitute cefotaxime 1 g (child: 50 mg/kg to 1 g) i.v. 8 hourly or ceftriaxone 1 g (child: 100 mg/kg to 1 g) i.v. once daily if Gram negative bacilli suspected; aggressive expectoration, chest physiotherapy, postural drainage; surgery (drainage of empyema secondary to lung abscess if tube drainage is inadequate; to differentiate lung abscess from carcinoma if other approaches are unsuccessful; life-threatening hemoptysis)

Pseudomonas aeruginosa: oral ciprofloxacin for 12 w

PULMONARY GANGRENE

Agents: *Bacteroides*, *Peptostreptococcus*

Diagnosis: culture of biopsy

Treatment: chloramphenicol

***RESPIRATORY SYNCYTIAL VIRUS* INFECTIONS**: conditions include bronchitis, cold, croup, bronchiolitis, pneumonia and pneumonitis; major cause of lower respiratory tract infection in young children; most frequent nosocomial infection on pediatric wards

Agent: respiratory syncytial virus

Diagnosis: culture, EIA (Vidas sensitivity 93%, specificity 94%), direct immunofluorescence (sensitivity 66%, specificity 73%) of nasopharyngeal aspirate in first 3-4 d

Treatment: ribavirin aerosol

BORNHOLM DISEASE (EPIDEMIC PLEURODYNIA)

Agent: *coxsackievirus B1-5*, *echovirus 6*

Diagnosis: viral culture of throat and nasal swabs, faeces and CSF in tissue culture, suckling mice; serology (neutralisation); biochemistry normal; no neutrophilia

Treatment: non-specific

ORNITHOSIS (BEDSONIA PNEUMONIA, PAPAGEIENKRONKHEIT, PARROT FEVER, PSITTACOSIS, PSITTACOSIS PNEUMONIA): ≈ 80 notified cases/y in Australia (≈ 80% in Victoria); incidence 0.05/100,000 in USA; incubation period 6-15 d; adults; person-to-person transmission rare; transmitted by excreta of infected birds, usually psittacines; usually acute pneumonitis but has been associated with embolisms and infective endocarditis

Agent: *Chlamydia psittaci*

Diagnosis: variable fever, infrequent rigours, productive cough with pleuritic chest pain; upper respiratory symptoms present or absent; pleural effusion rare; sputum mucoid, bloody, no bacteria on stain; headache, myalgias prominent; macular rash, splenomegaly may be present; patchy abnormal densities in lower segments of lower lobes; exposure to parrots or turkeys; complement fixation; culture of sputum; direct fluorescent antibody staining of respiratory secretions or tissue; microimmunofluorescence; PCR; abnormal liver function tests in 50% of cases, serum sodium ≤ 130 mmol/L in 44%, serum albumin ≤ 2.5 g/dL in 44%, blood urea ≥ 7 mmol/L in 11%; white cell count ≥ 15,000/μL in 83% of cases

Treatment: doxycycline 200 mg orally at once, then 100 mg orally daily for 14 d (not in children), roxithromycin for 14 d

Prevention and Control: eliminate contact with infected birds

Q FEVER: case-fatality rate < 1%; incubation period 14-35 d; adults; work in abattoir or on farm; ≈ 500 notified cases/y in Australia (≈ 57% in Queensland)

Agent: *Coxiella burnetii*

Diagnosis: pleural effusion rare; chest X-ray normal or patchy consolidation at bases of lungs; inflammatory apical lung disease by radioactive isotope scan; indirect immunofluorescent antibody titre; complement fixation test (phase 2, second to fourth weeks); culture of blood, urine

Treatment: doxycycline 100 mg orally 12 hourly for 14 d (not < 8 y), chloramphenicol 12.5 mg/kg to 500 mg orally or i.v. 6 hourly for 14 d

Prophylaxis (Postexposure): doxycycline 2.5 mg/kg to 100 mg orally 12 hourly

PULMONARY TUBERCULOSIS (COMPLICATED PRIMARY TUBERCULOSIS, FIBROCASEOUS PULMONARY TUBERCULOSIS, KOCH DISEASE, POST-PRIMARY PULMONARY TUBERCULOSIS, SECONDARY PULMONARY TUBERCULOSIS): infectious disease of the lung; may arise either by direct extension of a poorly localised 'primary tuberculous infection' or by reactivation of a quiescent lesion resulting from such an infection; if poorly localised, primary infection may occasionally progress to other areas of the lung (progressive primary pulmonary tuberculosis), sometimes leading to cavitation or extrapulmonary dissemination; in most cases, however, primary tuberculous infection heals, with or without calcification, or remains quiescent; when such a primary focus is

reactivated, or if exogenous superinfection occurs, characteristic inflammatory reaction takes place with tubercle formation, tissue necrosis (caseation), cavitation, fibrosis and, sometimes, calcification; pulmonary tuberculosis may lead to any of the following conditions: infiltrative tuberculosis of the lung, nodular tuberculosis of the lung (tuberculoma), tuberculosis of the lung with cavitation, tuberculous pneumonia, bronchial tuberculosis (endobronchial tuberculosis, tuberculosis of the bronchus, tuberculous bronchitis), tuberculous bronchiectasis, tuberculous pneumothorax, tuberculous pleuritis (pleural tuberculosis, tuberculosis of the pleura, tuberculous pleurisy), tuberculous emphysema; 85-90% of tuberculosis cases (+ 2% pleural)

Agents: *Mycobacterium tuberculosis*, *Mycobacterium bovis* (from raw cow's milk; now virtually eliminated in many countries); *Mycobacterium kansasii, Mycobacterium avium-intracellulare* (cavitary and nodular disease in immunocompromised, diffuse pulmonary disease (hot tub lung) in immunocompetent), *Mycobacterium fortuitum* (emerging pathogen in AIDS), *Mycobacterium chelonae, Mycobacterium szulgai, Mycobacterium xenopi* and, infrequently, *Mycobacterium gordonae, Mycobacterium malmoense, Mycobacterium scrofulaceum, Mycobacterium simiae* cause clinically indistinguishable conditions

Diagnosis: unresolved pneumonia, persistent cough, unexplained fever; contact; epidemiological history; unilateral or bilateral upper lobe or apical or multiple infiltration ± cavitation or consolidation or calcification (*Mycobacterium fortuitum* and *Mycobacterium chelonae*: 71% patchy, 38% bilateral, 17% cavitating, 8% empyema, 8% middle lobe infiltrate); nontuberculous mycobacterial infections (especially those caused by *Mycobacterium kansasii* and *Mycobacterium intracellulare*) have a more indolent course and are more common in older white males with underlying disease; Ziehl-Neelsen stain (specificity 99.9%; 46% of *Mycobacterium tuberculosis*, 22% of other *Mycobacterium* positive; 59% abundant organisms in culture, 50% few organisms in culture positive; 57% cavitating, 32% non-cavitating positive) and culture of voluntary or induced sputum (positive in 85-90% of cases), laryngeal swab or aspirate, bronchial swab or lavage, gastric lavage, pleural fluid or pus (Bactec: 95% smear positive specimens culture positive in 5-8 d, 72% smear negative specimens culture positive in 4-17 d, sensitivity testing 4-7 d with 91% agreement with conventional, identification of 99-100% of *Mycobacterium tuberculosis* in 5 d; conventional: 91% smear positive specimens culture positive in 18-19 d, 89% smear negative specimens culture positive in 18-43 days, sensitivity testing 14-32 d); DNA probe; tuberculin test; interferon gamma assay, ELISPOT; *Mycobacterium tuberculosis* gives anemia (acute hemolytic in miliary tuberculosis), raised ESR and neutrophilia, becoming lymphocytosis in the acute disseminated stage and monocytosis during healing; *Mycobacterium kansasii* gives severe anemia, leucopenia with white cell count < 500/μL, gross thombocytopenia

Differential Diagnosis: blastomycosis (skin lesions often present), histoplasmosis (culture and serology helpful), coccidioidomycosis (history of residence or travel to endemic areas), lung abscess (location and predisposing factors different; cavity usually thick-walled with air-fluid level), cavitating bronchogenic carcinoma (history, cytology and biopsy of tissue)

Treatment: vitamin A, zinc

Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium xenopi: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Mycobacterium kansasii: isoniazid 10 mg/kg to 300 mg orally daily + rifampicin 10 mg/kg to 600 mg orally twice daily + ethambutol 15 mg/kg orally (not < 6 y) daily for 18 mo and 12 mo negative sputum cultures

Mycobacterium szulgai: rifampicin + ethambutol + ethionamide or streptomycin

Mycobacterium fortuitum*, *Mycobacterium chelonae: 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

Mycobacterium avium-intracellulare: ethambutol 15 mg/kg orally daily or 25 mg/kg orally 3 times weekly (not < 6 y) + clarithromycin 12.5 mg/g to 500 mg orally 12 hourly daily or 3 times weekly or azithromycin 10 mg/kg to 500 mg orally daily or 10 mg/kg to 600 mg orally 3 times weekly + rifampicin 10 mg/kg to 600 mg orally daily or 3 times weekly or rifabutin 5 mg/kg to 300 mg orally daily

Prophylaxis (Treatment of Latent Infection):

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally daily for 9 mo if tuberculin skin test > 5 mm in patient who has not had BCTG and no evidence of active disease [+ pyridoxine 25 mg (breastfed baby: 5 mg) with each dose]

***Mycobacterium avium* complex in HIV Infection (CD4 Cell Count < 50/μL):** azithromycin 1.2 g orally weekly or clarithromycin 500 mg orally 12 hourly or rifabutin 300 mg orally daily

PULMONARY HISTOPLASMOSIS: clinical state varies from asymptomatic (usually in acute, 20% of chronic) to tuberculosis-like to widespread ulceration; pericarditis, mediastinal granuloma, mediastinal fibrosis, histoplasmoma rare complications; chronic infection with structural defect (males over 50 y; underlying chronic bronchitis and/or emphysema; respiratory insufficiency usual cause of death; mortality 55% untreated, 30% treated)

Agent: *Histoplasma capsulatum*

Diagnosis: cough, malaise, easy fatigability, weight loss, low grade fever; chest pain, deep and aching, suggestive of carcinoma, and hemoptysis (usually in cavitary disease) in ≈ 1/3 of chronic cases; dyspnea with progression; chest X-ray mimics tuberculosis; fungal culture of sputum at 25°C and 37°C; histoplasmin skin test of no diagnostic help; complement fixation test diagnostic in 35%, not helpful in determining prognosis or need for treatment

Treatment: patients with chronic disease and patients with acute disease and a good history of exposure to the organism, acute ill with an illness of several weeks duration, a chest X-ray with diffuse involvement, or a positive culture or fourfold or higher rise in the complement fixation test should be treated with amphotericin B or ketoconazole

PULMONARY CRYPTOCOCCOSIS: next to meningitis, most common clinical manifestation of cryptococccal infection

Agent: *Cryptococcus neoformans*

Diagnosis: fever in 66% of cases, chest pain in 45%, weight loss in 35%, dyspnea in 25%, night sweats in 25%, cough in 15%, haemoptysis in 7%, 15% asymptomatic; chest X-ray (predilection for lower lung fields; lesions range from solitary mass to diffuse infiltrates or scattered miliary nodules; cavitation, calcification, hilar lymphadenopathy, pulmonary collapse unusual); microscopy and culture of bronchoalveolar lavage (100% positive), open-lung biopsy (100% positive), pleural fluid (50% positive), sputum (35% positive), bronchoscopy (35% positive)

Treatment: indicated if progression of chest X-ray findings, symptoms of increasing severity, stable disease in patient who is susceptible to dissemination (eg., malignancy, corticosteroid therapy); not indicated in asymptomatic carriers (eg., isolation of organism from sputum of patients with chronic bronchitis)

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

BAGASSOSIS AND FARMER'S LUNG

Agents: *Saccharopolyspora rectivirgula, Aspergillus fumigatus, Aspergillus niger, Aspergillus terreus, Aspergillus flavus, Aspergillus clavatus, Aspergillus nidulans, Penicillium, Coniosporum corticale, Mucor, Candida, Curvularia lunata* (rare)

Diagnosis: recurrent bouts of symptoms of acute bronchitis or pneumonia, with pulmonary infiltrates and eosinophilia in all cases, asthma in 95%, haemoptysis (blood-tinged) in 85%; bronchograms demonstrating proximal saccular bronchiectasis; serum precipitins (positive in 90%); skin test (types I and III; positive in 95% of cases of allergic bronchopulmonary aspergillosis); RAST test (positive in nearly all cases of allergic bronchopulmonary aspergillosis); organism cultured from sputum in 60% of cases

Allergic Bronchopulmonary Aspergillosis: double immunodiffusion (sensitivity > 10 μg/mL), ELISA (sensitivity 10-1000 ng/mL), immunoCAP (sensitivity > 0.35 kUA/L), Western blot (sensitivity 100-2000 ng/mL)

Differential Diagnosis: cystic fibrosis, tuberculosis, cancer, eosinophilic pneumonia, mucous plug, atelectasis, bronchiectasis

Treatment: prednisolone 0.5 mg/kg daily as a single dose for 2 w or until complete clearing of chest X-ray, then 0.5 mg/kg orally on alternate days for 2-3 mo then, monitoring IgE antibodies, taper off dose as appropriate; repeat chest X-ray 4 monthly X 6, 6 monthly X 4, then yearly if no exacerbations; serum IgE monthly for 2 y,

then bimonthly; pulmonary function tests yearly; resume prednisolone therapy if significant worsening of symptoms, chest X-ray or pulmonary function tests, or significant increase in total serum IgE

'COIN LESIONS'

Agent: *Dirofilaria immitis*

Diagnosis: primarily radiological; contact with dogs; rarely, microfilaria seen in sputum

Treatment: none required, as adult worms do not survive in humans

HEMOPTYSIS

Agents: may occur in acute pneumonia (17% of *Legionella* cases, 16% of *Streptococcus pneumoniae*, 3% of *Mycoplasma pneumoniae*), in 73% of cases of *Paragonimus (P.africanus, P.westermani)* infections, 11% of psittacosis cases and 3% of brucellosis, also in pulmonary tuberculosis, invasive aspergillosis, *Ascaris lumbricoides* infection, strongyloidiasis, Crimean-Congo hemorrhagic fever, echinococcosis, other infections and conditions unrelated to infection (eg., carcinoma, rupture of blood vessels due to trauma or inherent fragility)

Diagnosis: micro and culture of sputum; serology (complement fixation test); isolation of virus from blood; examination of stools for ova and parasites

Paragonimus: pneumonitis, cough, hemoptysis, chest pain, pleurisy, low grade fever, breathlessness, epilepsy, possible development of bronchiectasis and lung abscesses; may simulate tuberculosis or coexist with it; metastatic lesions in other organs, including bone; geographic history (*Paragonimus* common in Far East; also in W Africa and Central S America); dietary history (eating undercooked or raw crabs or shrimp); abnormal chest X-ray (infiltration, cavities, pleural effusion) in 80% of cases; ova in aspirate, puncture, biopsy, stool, sputum; eosinophilia; hemoglobin may be decreased; serology by complement fixation test

Treatment:

Paragonimus: praziquantel 25 mg/kg orally 8 hourly for 2 consecutive days (90% cure rate), bithionol 30-50 mg/kg orally on alternate days for 10-15 d

Others: dependent on agent; resection of nodules essential for management of invasive aspergillosis

HANTAVIRUS PULMONARY SYNDROME: severe pulmonary illness; case-fatality ratio 40-50%; carried by deer mouse (*Peromyscus maniculatus*) and other rodents; Argentina, Brazil, Canada, Chile, Panama, Paraguay, Peru, USA (especially Southwest)

Agent: *sin nombre virus, New York virus, Bayou virus, Black Creek Canal virus, Andes virus*

Diagnosis: 3-4 d prodrome of fever, myalgia, malaise, nausea, vomiting, abdominal pain, occasional dizziness and vertigo; then tachypnea, tachycardia, hypotension, hypoxemia, interstitial pulmonary markings, pulmonary edema, severe respiratory compromise; bilateral infiltrates; thrombocytopenia, immunoblasts, haemoconcentration; serology

Treatment: supportive

OTITIS MEDIA: 2% of new episodes of illness in UK; 2.6% of ambulatory care visits in USA; 5-7M cases/y in US; $\approx$ 15% of infants have an attack by 6 mo, $\approx$ 75% by 2 y (25-30% $\geq$ 3 attacks by this age), > 90% by 7 y; hearing loss and impaired language development may occur as sequelae

Agents: 66% mixed bacterial and viral, 30-45% *Haemophilus influenzae* (5-10% of isolates type b), 28-55% *Streptococcus pneumoniae,* 5-10% *Moraxella catarrhalis*, anaerobes, *Pseudomonas aeruginosa* (chronic and complicating endotracheal intubation and mechanical ventilation), *Streptococcus pyogenes*, *Staphylococcus aureus*, *Neisseria meningitidis* (1% of meningococcal infections), other *Neisseria* species (in infants); typically with viral coinfection: respiratory syncytial virus (in 39% of infected pre-school children; treatment failure in 30% of cases with bacterial coinfection), adenovirus (in 32% of infected pre-school children; treatment failure in 25% of cases with bacterial coinfection), influenza A (in 28% of infected pre-school children), influenza B (in 17% of infected pre-school children, 9% of infected school-age children), parainfluenza (in 16% of infected pre-school children), enteroviruses (in 16% of infected pre-school children; treatment failure in 17% of cases with bacterial coinfection), rhinovirus (in 10% of infected pre-school children; treatment failure in 78% of cases with bacterial coinfection), measles (in 4-22% of measles cases), echovirus 9 (in 10% of cases), *human human cytomegalovirus* (treatment failure in 17% of cases with bacterial coinfection); also *Corynebacterium bovis* (rare), *Mycobacterium tuberculosis* (chronic draining), Gram negative enteric bacilli (nosocomial), *Moraxella lacunata*, *Achromobacter xylosoxidans* (nosocomial and community acquired chronic), *Haemophilus haemoglobinophilus, Streptococcus canis, Mycoplasma pneumoniae* (bullous myringitis); male sex, family members with acute otitis media, child care outside home, parental smoking, not being breastfed, and pacifier use risk factors.

Diagnosis: acute onset of pain in ear, tugging of ear lobes, fever, otorrhoea, vertigo, disturbed sense of balance, feeding difficulties, night waking; pneumatic otoscopy (effusion characterised by bulging of the tympanic membrane, limited or absent movement of the tympanic membrane, air-fluid level behind the tympanic membrane or perforation of the tympanic membrane with otorrhoea; inflammation characterised by distinct erythema of the tympanic membrane or distinct otalgia); culture of ear swab if eardrum ruptured, otherwise tympanocentesis specimen; serology

Treatment: paracetamol 20 mg/kg for pain relief; topical benzocaine; laser-assisted myringotomy

Acute Bacterial with Systemic Features or Child < 6 mo:

Child < 2 y, Treated with Antibiotics within Previous 3 mo or Attending Day Care or If Unresponsive to Amoxycillin: amoxycillin-clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 8 hourly for 5-7 d

Others: amoxycillin 15 mg/kg to 500 mg orally 8 hourly for 5 d or 30 mg/kg to 1 g orally 12 hourly for 5 d

Penicillin Hypersensitive: cefuroxime 10 mg/kg to 500 mg orally 12 hourly for 5 d, cefaclor 10 mg/kg to 250 mg orally 8 hourly for 5 d; cotrimoxazole 4/20 mg/kg to 160/800 mg/kg orally 12 hourly for 7-10 d

Remote Areas: procaine penicillin 50 mg/kg to 1.5 g i.m. once daily for 5 d, bicillin i.m. on days 1 and 3 or daily for 2-5 d

Chronic Suppurative: suction under direct vision or dry mopping with rolled tissue spears or equivalent 6 hourly until ear canal dry; oral antibiotics as above + dexamethasone 0.05% + framycetin 0.5 % + gramicidin 0.05% ear drops 3 drops instilled into ear 6 hourly for 7 d

Streptococcus: phenoxymethylpenicillin 500 mg orally 6 hourly (child: 75 mg/kg orally daily in 3 divided doses) for 7-10 d

Haemophilus*, *Moraxella*, *Neisseria: amoxycillin-clavulanate 500/125 mg orally 8 hourly (< 40 kg: 40/10 mg/kg daily in 3 divided doses) for 10 d, cotrimoxazole 160/800 mg (6 w - 5 mo: 20/100 mg; 6 mo - 5 y: 40/200 mg; 6-12 y: 80/400 mg) orally 12 hourly for 7-10 d, cefaclor 250-500 mg orally 8 hourly (child: 40-60 mg/kg orally daily in 3 divided doses) for 7-10 d

Corynebacterium bovis: erythromycin + rifampicin

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Other bacteria: ticarcillin + gentamicin

Viruses: non-specific, but pneumococcal infection may supervene

Chronic (> 6 w) Discharging: ciprofloxacin or (dexamethasone 0.05% + framycetin 0.5% + gramicidin 0.005%) ear drops 3 drops 6 hourly until middle ear free of discharge for at least 3 d; at least daily wash with water, acetic acid 0.25% or povidone iodine 0.5% solution until cured; 4 times daily ear toilet with rolled paper spears repeating until ear is dry), followed each time by acetic acid 1% drops or by boric acid drops in acetic acid

Prophylaxis: identification and correction of underlying causes and risk factors (smoke exposure, group child care, allergic rhinitis, adenoid disease, cleft palate, Down syndrome); insertion of typanostomy tubes; amoxycillin 10-20 mg/kg orally in 2 divided doses or sulphisoxazole 80-100 mg/kg orally daily in 2 divided doses; acetic acid ear drops; polymyxin and neomycin ear drops; intranasal virosomal influenza vaccine

Neisseria meningitidis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

Mastoiditis: formerly worldwide in childhood but now, due to effective treatment of otitis media, almost eliminated in developed countries

Agents: *Haemophilus influenzae* (3% of non-bacteremic invasive *Haemophilus influenzae* infections in older children and adults), *Staphylococcus aureus*, anaerobes, *Burkholderia cepacia* (occasional), *Streptococcus pneumoniae, Streptococcus pyogenes, Pseudomonas,* anaerobes
Diagnosis: otitis media + pain and tenderness over mastoid process; otoscopy; computed tomography; culture of surgical specimen
Treatment:

Acute: amoxycillin 200 mg/kg i.v. daily in divided doses + cloxacillin/flucloxacillin 200 mg/kg i.v. daily in divided doses; dicloxacillin; cefuroxime; surgery for abscess or osteomyelitis

Chronic: ceftazidime + clindamycin; tobramycin + ticarcillin-clavulanate; surgery required

Prophylaxis (Otitis-Prone Child): sulphamethoxazole 25 mg/kg orally daily at bedtime

Chapter 2

Infections of the Gastrointestinal Tract and Associated Structures

Angular Cheilitis

Agents: usually *Candida albicans*; also iron or riboflavin deficiency
Diagnosis: swab culture
Treatment: miconazole 2% gel or nystatin 100,000 U/g ointment topically to lesions 2-3 times daily for at least 2 w

Mouth Lesions

Agents: chickenpox, measles, molluscum contagiosum, human papillomavirus in 1.2% of HIV patients, *human human cytomegalovirus* in AIDS, *Lymphocryptovirus* (oral hairy leucoplakia in AIDS), enteroviruses, *Simplexvirus*, *Moraxella osloensis, Candida albicans* (pseudomembranous, erythematous, hyperplastic)
Diagnosis: viral culture and cytology of swab of lesions; serology; bacterial and fungal culture
Treatment:

Human Papillomavirus: surgical removal of lesion and surrounding tissue

***Human human cytomegalovirus*:** valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria $\leq$ 2+ and creatinine clearance $\geq$ 55 mL/min) then as above every 2 w

Hairy Leukoplakia: high dose aciclovir

***Simplexvirus*:**

Herpes labialis: penciclovir cream

Internal Lesions: see **Acute Herpetic Gingivostomatitis**

Candida albicans:

Pseudomembranous and Erythematous: miconazole 2% gel (< 1 y: 1.25 mL; > 1 y: 2.5 mL) orally 6 hourly for 7-14 d, amphotericin 10 mg lozenge orally 6 hourly for 7-14 d (remove dentures while sucking if worn), nystatin suspension 100 000 units/mL 1 mL orally 6 hourly for 7-14 d; soak dentures in 1:100 sodium hypochlorite solution at night

Hyperplastic: fluconazole 3 mg/kg to 50-100 mg orally daily for 10-14 d, ketoconazole 5 mg/kg to 200 mg orally daily for 10-14 d

Others: non-specific

Mouth Ulcers

Agents: many aphthous (cause unknown; may be linked to nutritional or physiological factors or hypersensitivity to oral streptococci); syphilis, necrotising ulcerative gingivostomatitis, *Mycobacterium tuberculosis*, *Simonsiella,* viruses especially coxsackievirus and *Simplexvirus*; also occurs in Reiter syndrome, Crohn's disease and ulcerative colitis and as a response to radiation and some drugs
Diagnosis: dark ground illumination, Gram stain or simple stain, viral and mycobacterial culture of tissue fluid and swab of lesions; direct immunofluorescence for herpes; serology; skin testing with autogenous streptococcal vaccine
Treatment:

Aphthous: saline rinse after each meal and at bedtime; chlorhexidine 0.2% mouthwash 10 mL 8 hourly, held in mouth 1 min; triamcinolone acetonide 0.1% paste topically 8 hourly, betamethasone valerate 0.05% ointment

More Severe: betamethasone dipropianate 0.05% ointment or cream

Major Ulceration: prednisolone or prednisone 20 mg orally daily for 5 d

AIDS: thalidomide 200 mg daily for 4 w

Syphilis, *Simonsiella*: penicillin

Tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Severe Herpes: famciclovir 125 mg orally 12 hourly for 5 d, valaciclovir 500 mg orally 12 hourly for 5 d, aciclovir 5 mg/kg to 200 mg orally 5 times daily for 5 d; if unable to swallow, aciclovir 5 mg/kg i.v. 8 hourly for 5 d

Others: salt + sodium bicarbonate mouthwashes

MOUTH ABSCESS

Agents: *Rothia dentocariosa, Streptococcus milleri*

Diagnosis: culture of swab

Treatment: penicillin

NECROTISING ULCERATIVE GINGIVOSTOMATITIS (ACUTE INFECTIOUS GINGIVOSTOMATITIS, FETID STOMATITIS, FUSOSPIROCHAETAL STOMATITIS, PLANT ULCER, PLANT-VINCENT DISEASE, PLANT-VINCENT STOMATITIS, PUTRID SORE MOUTH, PUTRID STOMATITIS, SPIROCHAETAL STOMATITIS, STOMATITIS ULCEROMEMBRANACEA, STOMATITIS ULCEROSA, TRENCH MOUTH, ULCERATIVE STOMATITIS, ULCEROMEMBRANOUS STOMATITIS, VINCENT DISEASE, VINCENT INFECTION, VINCENT STOMATITIS): acute ulcerative necrotising condition of gum margins and other parts of mouth, often with pseudomembrane formation; may be restricted to gingival margins (necrotising ulcerative gingivitis, acute septic gingivitis, acute ulcerative gingivitis, acute ulceromembranous gingivitis, acute ulcerous gingivitis, fusobacillary gingivitis, fusospirillary gingivitis) or involve only parts of mouth other than gums (necrotising ulcerative stomatitis); rarely, may progress and become gangrenous (cancrum oris, fusospirochaetal gangrene, noma, stomatitis gangrenosa)

Agents: probably a mixed infection with *Leptotrichia buccalis, Treponema vincentii* and possibly other *Treponema*

Diagnosis: simple stain of swab

Treatment: local debridement; metronidazole 10 mg/kg to 400 mg orally 12 hourly for 5 d + povidone iodine mouthwash diluted as directed 10 mL rinsed in mouth for at least 15 s 6 hourly or chlorhexidine 0.2% mouthwash 10 mL rinsed in mouth for 1 min 8-12 hourly or 0.12% mouthwash 15 mL rinsed in mouth 1 min 8-12 hourly

More Severe Or Unresponsive: metronidazole 10 mg/kg to 400 mg orally 12 hourly + phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly or amoxycillin 10 mg/kg to 500 mg orally 8 hourly or (penicillin hypersensitive) clindamycin 7.5 mg/kg to 300 mg orally 8 hourly for 5 d

GEOGRAPHIC TONGUE, HAIRY TONGUE, BLACK HAIRY TONGUE

Agents: successive stages of papillary hypertrophy due to toxic effects of a number of agents; black colour due to overgrowth of anaerobes; often confused with fungal infection in later stages

Diagnosis: appearance

Treatment: avoidance of precipitating factors if known; salt and sodium bicarbonate mouthwashes

LINGUAL CELLULITIS: extremely rare; following minor local trauma in neutropenics

Agents: anaerobic streptococci, *Pseudomonas aeruginosa*

Diagnosis: blood cultures

Treatment: ticarcillin-clavulanate

ACUTE HERPETIC GINGIVOSTOMATITIS

Agent: *Simplexvirus*

Diagnosis: viral culture of swab of lesions, throat swab or washing in tissue culture; cytology and immunofluorescence or electron microscopy of scraping from base of vesicle if accessible

Treatment: famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

GINGIVITIS, PERIODONTITIS

Agents: commonest non-contagious disease; *Porphyromonas gingivalis* (dominant organism in rapidly progressive periodontitis), *Actinobacillus actinomycetemcomitans* (dominant organism in juvenile periodontitis), mixed anaerobes (fusospirochaetal; dominant organisms in adult periodontitis), *Porphyromonas asaccharolytica, Prevotella intermedius, Prevotella melaninogenica*, *Capnocytophaga*, *Campylobacter concisus, Treponema denticola, Bacteroides forsythus*; HIV (linear gingival erythema, which may lead to necrotising ulcerative periodontitis and/or stomatitis); also due to cyclosporin, phenytoin, calcium channel antagonists

Diagnosis: Gram or simple stain, anaerobic culture and culture in increased CO_2 of swab

Treatment: local dental care to control bacterial plaque; povidone iodine irrigation; debridement if necrosis; chlorhexidine 0.2% mouthwash 10 mL rinsed in mouth for 1 min 8-12 hourly or 0.12% mouthwash 15 mL rinsed in mouth for 1 min 8-12 hourly

Linear Gingival Erythema: professional removal of plaques and daily rinses with chlorhexidine gluconate

PERICORONITIS, ROOT CANAL INFECTION

Agents: mixed normal mouth flora

Diagnosis: clinical; culture usually not helpful

Treatment: local dental care in absence of tooth abscess; vigorous warm mouth rinses with saline or chlorhexidine 0.2%; topical povidone iodine

TOOTH ABSCESS

Agents: mixed oral flora

Diagnosis: culture of aspirated pus

Treatment: removal of infected pulp tissue ± drainage; if systemic signs and symptoms, phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly or amoxycillin 10 mg/kg to 500 mg orally 8 hourly for 5 d; if more severe or unresponsive, + metronidazole 10 mg/kg to 400 mg orally 12 hourly for 5 d or amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for 5 d alone

Penicillin Hypersensitive: clindamycin 7.5 mg/kg to 300 mg orally 8 hourly for 5 d

OTHER DENTAL INFECTIONS

Agents: various anaerobes

Diagnosis: culture of deep aspiration or surgical specimen

Treatment: penicillin, clindamycin, chloramphenicol

SALIVARY CALCULI

Agent: *Actinomyces*

Diagnosis: anaerobic culture

Treatment: removal; penicillin if necessary

PAROTITIS AND SUBMANDIBULAR SIALADENITIS

Agents: mumps virus (epidemic parotitis), coxsackievirus, parainfluenza 1 and 3, lymphocytic choriomeningitis virus, influenza A, *Staphylococcus aureus* (nosocomial and xerostomia-inducing process), streptococci, anaerobes, enteric Gram negative bacilli, *Mycobacterium tuberculosis*, *Actinomyces*, *Actinobacillus actinomycetemcomitans* (uncommon), *Burkholderia pseudomallei*, *Pseudomonas aeruginosa,* also in 4% of Rocky Mountain spotted fever cases; also neoplastic, cysts, drugs (iodides, bromides, phenothiazines, propylthiouracil, isoproteneol), obstruction, malnutrition, gout, uremia, sarcoidosis, Mikulicz's disease, Sjorgren's syndrome, cystic fibrosis; may be confused with lymphadenopathy, masseter hypertrophy, dental abscess

Diagnosis: pain, swelling, dysphagia, tense swelling over parotid area, tenderness, pain on opening mouth; viral culture of saliva, throat swab, urine; serology (complement fixation test, haemagglutination inhibition); increased serum amylase; bacterial culture of purulent discharge from Stensen's duct or surgical drainage material

Treatment: early surgical drainage may be necessary in suppurative sialadenitis

Viral: none

Staphylococcus aureus: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly then 12.5 mg/kg to 500 mg orally 6 hourly for total 10 d, clindamycin 10 mg/kg to 450 mg i.v. 8 hourly then 10 mg/kg to 450 mg orally 8 hourly for total 10 d, lincomycin 15 mg/kg to 600 mg i.v. 8 hourly then clindamycin 10 mg/kg to 450 mg orally 8 hourly for total 10 d

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Burkholderia pseudomallei: early surgical drainage + cotrimoxazole + ceftazidime or meropenem or imipenem

Other Bacteria: cloxacillin + aminoglycoside + clindamycin or penicillin if anaerobes isolated or suspected; rehydration

GASTROINTESTINAL TRACT INFECTIONS: Even under the best of conditions, a specific agent is not found in the majority of cases of gastrointestinal tract disturbances. This may be due to a number of factors: infection due to an uncommon and unlooked-for organism or to an organism not yet implicated in gastrointestinal tract infection; deficiencies in transport and/or isolation procedures for some organisms; the sporadic nature of the presence of some organisms in faeces; the existence of a dietary or physiological (eg., lactase deficiency, gluten sensitivity, Crohn's disease, etc) cause unrelated to infection

OESOPHAGITIS: mainly in immunocompromised patients; 0.1% of ambulatory care visits in USA

Agents: *Mycobacterium tuberculosis*, *Candida*, *Simplexvirus*, enteroviruses, *human human cytomegalovirus*; also non-infectious ulcers in AIDS

Diagnosis: dysphagia, odynophagia, retrosternal pain; esophagoscopy; barium swallow; KOH smear, viral culture and monoclonal antibody immunofluorescence to *Simplexvirus* and *human cytomegalovirus* on esophageal brushings; hematoxylin and eosin stain, Grocott methenamine silver stain, Ziehl-Neelsen stain, monoclonal antibody immunofluorescence to *Simplexvirus*, *human cytomegalovirus*, mycobacterial culture, fungal culture and viral culture on esophageal biopsy specimens

Tuberculosis: positive tuberculin test, mediastinal adenopathy

Candida: recent onset of retrosternal pain on swallowing + oral candidiasis diagnosed by gross appearance of white patches or plaques on an erythematous base or by the microscopic appearance of fungal mycelial filaments from a specimen cultured from oral mucosa

Treatment:

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Candida: fluconazole 5 mg/kg to 200 mg orally initially then 2.5 mg/kg to 100 mg daily for 14 d or itraconazole 200 mg capsule orally daily or 100 mg (10 mL) oral suspension twice daily for 14 d; if resistant, voriconazole 200 mg orally 12 hourly for 14 d or amphotericin B desoxycholate 0.5 mg/kg i.v. daily for 14 d

Repeated Episodes in HIV Infection: fluconazole 100 mg orally daily, itraconazole 200 mg orally daily, ketoconazole 200 mg orally daily

Simplexvirus: as for **HERPETIC GINGIVOSTOMATITIS**

Human cytomegalovirus: valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly or 180 mg/kg/d by continuous i.v. infusion for 14 d then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria ≤ 2+ and creatinine clearance ≥ 55 mL/min) then as above every 2 w

Non-infectious: prednisone

GASTRITIS, DUODENAL ULCER, PEPTIC ULCER, DYSPEPSIA: 0.5% of ambulatory care visits in USA

Agents:

Simple Gastritis, Duodenal Ulcer, Peptic Ulcer, Dyspepsia: *Helicobacter pylori;* peptic ulcer also due to NSAID ingestion; also gastritis and antral obstruction due to *human cytomegalovirus* in AIDS and posttransplantation

Emphysematous Gastritis: 22% *Escherichia coli*, 22% streptococci, 19% *Enterobacter,* 11% *Pseudomonas aeruginosa*, others; mortality 61%, gastric constrictions 21%

Diagnosis:

***Helicobacter pylori*:** silver or Gram stain, phase contrast microscopy and culture of multiple gastric mucosal biopsies on chocolate agar or brain heart infusion agar with and without nalidixic acid (50 mg/L), vancomycin (3 mg/L) and trimethoprim (5 mg/L) (histology sensitivity 88-95%, specificity 90-95%, very readily available, very expensive; culture 80-90% sensitivity, 95-100% specificity, less readily available, expensive); ^{13}C urea breath test (sensitivity 90-95%, specificity 90-95%, very readily available, expensive); ^{14}C urea breath test (sensitivity 86-95%, specificity 86-95%, readily available, less expensive; give drink containing 4 g citric acid before test if taking proton pump inhibitor), antigen in stool test (sensitivity 88-100%, specificity 70-96%, less readily available, less expensive); Stat Simple fingerstick antibody test (sensitivity 60-90%, specificity 70-85%, very readily available, relatively inexpensive); ELISA (sensitivity 80-95%, specificity 80-95%, readily available, inexpensive); rapid urease test (sensitivity 90-95%, specificity 90-95%, very readily available, relatively inexpensive); Leukostix rapid leucocyte strip test (sensitivity 98%, specificity 77%); barium study; testing should not be done less than 4 w after cessation of antibiotics or bismuth compounds or 1-2 w after proton pump inhibitors; serological tests for antibodies are unsuitable for post-treatment testing because antibody titres may take months to fall

***Human cytomegalovirus*:** endoscopy with biopsy; PCR on blood

Emphysematous Gastritis: 37% ingestion of corrosive substances, 22% alcohol abuse; acute abdomen with systemic toxicity; X-rays show gas bubbles within stomach wall; computed tomography; culture of gastric aspirate

Treatment:

***Helicobacter pylori*:** omeprazole 20 mg orally 12 hourly or lansoprazole 30 mg orally 12 hourly for 7 d + clarithromycin 500 mg orally twice daily for 7 d + amoxycillin 1 g orally twice daily for 7 d or metronidazole 400 mg orally 3 times daily for 1 w

Treatment Failure: colloidal bismuth subcitrate 1 tablet (107.7 mg) chewed and swallowed 4 times daily for 2 w + tetracycline 500 mg 6 hourly for 2 w + metronidazole 200 mg orally 3 times daily and 400 mg orally at night for 2 w + omeprazole 20 mg or lansoprazole 30 mg or pantoprazole 40 mg twice daily for 14 d; rifabutin 300 mg 4 times/d + pantoprazole 40 mg twice a day + amoxycillin 1 g twice a day

***Human cytomegalovirus*:** valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria $\leq$ 2+ and creatinine clearance $\geq$ 55 mL/min) then as above every 2 w

Emphysematous Gastritis: i.v. fluid, nutritional support; tobramycin + imipenem; surgery as required

CONSTIPATION is mainly due to dietary causes (including in infant metabolic alkalosis) but also occurs in 26% of cases of cryptosporidiosis (after initial diarrhoea in 22%), in 18% of brucellosis cases and 5% of cases of subdural empyema, and also in botulism, diphyllobothriasis, *Entamoeba histolytica* and *Salmonella typhi* infections and (alternating with diarrhoea) in strongyloidiasis

BLOODY STOOLS occur in enterohemorrhagic *Escherichia coli* infections, amoebic dysentery, 60% of cases of shigellosis, 31% of acute schistosomiasis, 26% of *Campylobacter* enteritis, 21% of salmonellosis, 12% of enterotoxigenic *Escherichia coli* infections, 7% of typhoid fever, 4% of cholera, and also in necrotising enterocolitis and *Vibrio cholerae* non-01 infections; also in ulcerative colitis

FATTY STOOLS, when due to infectious causes, are usually due to *Giardia intestinalis*

ACUTE DIARRHOEA AND/OR VOMITING: 4% of new episodes of illness in UK; 99 million episodes/y among adults in USA (with 8 million doctor visits and 1.5% of hospitalisations; 85% of deaths in > 60 y)

Agents: due to infectious causes in 90% of cases; developed areas: 10-27% *Norovirus*, 8-50% *Rotavirus*, < 5% enteropathogenic *Escherichia coli* (atypical strains), 3-7% *Giardia intestinalis,* 3-4% *Cryptosporidium,* 2-52% *Salmonella*, 2% enteric adenovirus (< 2 y), 1-40% *Campylobacter*, 1-16% enterotoxigenic *Escherichia coli,* 1-4% *Shigella*, 1-4% *Yersinia,* 0.6% *Entamoeba histolytica*, 0.2% *Strongyloides, Vibrio, Aeromonas, Clostridium difficile, Bacteroides fragilis;* developing areas: 7-50% enterotoxigenic *Escherichia coli*, 5-45% *Rotavirus*, 5-16% *Shigella*, 5-10% enteric adenovirus (< 4 y), 5% *Strongyloides*, 4-10% *Cryptosporidium*, 4-8% enteropathogenic *Escherichia coli* (typical strains), 2-15% *Entamoeba histolytica*, 2-14% *Campylobacter*, 1-44% *Giardia lamblia*, 1-6% *Yersinia*, 1-2% *Norovirus*, 0-15% *Salmonella*, *Vibrio*, *Aeromonas*, *Clostridium difficile*, *Bacteroides fragilis*; AIDS: *Cryptosporidium*, *Microsporidium, Isospora belli, Pneumocystis jiroveci, Strongyloides, Entamoeba histolytica, Giardia lamblia, human cytomegalovirus*, *Mycobacterium avium-intracellulare*, *Mycobacterium tuberculosis*, *Salmonella*, *Campylobacter*, AIDS 'enteropathy'; acute diarrhoea may also be due to cancer of the colon and rectum, non-infectious food poisoning or ulcerative colitis; acute vomiting may also be caused by preformed toxins (vomitoxin, *Staphylococcus aureus* toxin, *Bacillus cereus* toxin, heavy metals, nitrites, *Aminita* mushrooms), acute nephritis, anemia, diabetic precoma, glaucoma, migraine, myocardial infarction, pregnancy and renal colic

Diagnosis: feces examination (ulcerative colitis: 90% polymorphonuclears + ≈ 10% eosinophils); collapsed patient: electrolytes and hematocrit; other investigations only if not resolved within 48 h

Treatment: dietary restriction; oral fluids and i.v. fluids in dehydration; *Lactobacillus* ≥ 10^{10} cfu ≥ twice daily; specific treatment as indicated

Diarrhoea: global incidence 4 billion/y; global morbidity 3-5 billion/y; global mortality 3-4 M/y; 90% simple diarrhoea (mainly viral (agents of **Epidemic Viral Diarrhoea** and echovirus 8, 19, 20, 22-24, 32) in industrialised countries, also bacterial and protozoal in less developed), 5-10% dysentery (*Shigella*, *Campylobacter jejuni,* enteroinvasive *Escherichia coli*), 3-4% protracted diarrhoea (≥ 14 d; enteropathogenic *Escherichia coli*, *Giardia lamblia*), 1% severe passing of rice water stools (*Salmonella* and enterotoxigenic *Escherichia coli* in industrialised countries, cholera and enteropathogenic *Escherichia coli* in less developed); as well as in enteric infections, diarrhoea occurs as a symptom in 61% of measles cases occurring in malnourished (13% bloody), in 57% of cases of neonatal listeriosis, in 41% of cases of Kawasaki syndrome (days 1-14), in 40% of cases of primary sepsis and 12% of wound infections due to *Vibrio vulnificus*, in 33% of cases of cranial epidural abscess, 31% of brain abscess and 10% of subdural empyema due to *Salmonella*, in 33% of cases of Korean hemorrhagic fever, in 30% of peritonitis, in influenza A (in 27% of cases) and B (in 35% of infected school-age children, 10% of infected pre-school children, 4% of infected adults), in 21% of cases of *Yersinia pseudotuberculosis* infections, 19% of cases of amoebic liver abscess, 19% of Rocky Mountain spotted fever (9% in first 3 d), 16% of brucellosis cases, and in AIDS, congenital malaria, Crimean-Congo hemorrhagic fever (liquid), Ebola hemorrhagic fever, grain itch, Lassa fever, Lyme disease (mild, watery), Marburg virus disease, plague (massive), psittacosis, toxic shock syndrome (84% profuse, watery at onset), Reye syndrome; also in chemical poisoning, gastroenteritis-type mushrooms (*Amanita, Phalloidin, Gyromitrin* toxin group) ingestion, in protein-energy malnutrition (non-bloody), and due to antibiotics and other medications or to diet

Diagnosis: feces micro and culture; unexplained abdominal pain and fever persisting or suggesting an appendicitis-like syndrome suggests *Yersinia enterocolitica;* bloody diarrhoea, especially if without fecal leucocytes, suggests enterohemorrhagic (shiga toxin-producing) *Escherichia coli* or amoebiasis (where leucocytes are destroyed by the parasite); ingestion of inadequately cooked seafood should prompt consideration of *Vibrio* infections or *Norovirus*; cytotoxigenic *Clostridium difficile* should be considered in diarrhoea associated with antibiotic use; persistence > 10 d with weight loss should prompt consideration of giardiasis or cryptosporidiosis; travel to tropical areas or consumption of untreated water increases the chance of enterotoxigenic *Escherichia coli* as well as viral (eg., Norwalk-like or rotaviral), parasitic (eg., *Giardia intestinalis*, *Entamoeba histolytica*, *Strongyloides*, *Cryptosporidium, Cyclospora cayetanensis*) and, if faecal leucocytes are present, invasive bacterial pathogens (eg. *Shigella*, *Salmonella*, *Campylobacter*); outbreaks should prompt consideration of *Staphylococcus aureus*, *Bacillus cereus, Anisakis* (incubation period < 6 h), *Clostridium perfringens* (incubation period 12-18 h), enterotoxigenic *Escherichia coli* or *Vibrio* (noninflammatory), *Salmonella*, *Campylobacter*, *Shigella,* enteroinvasive *Escherichia coli* infection, enterohemorrhagic *Escherichia coli*, *Vibrio parahaemolyticus, Yersinia enterocolitica* and *Entamoeba histolytica* (inflammatory); short incubation period also suggests metal or monosodium glutamate poisoning; neurologic symptoms suggest botulism, fish poisoning (scombroid, ciguatera, tetrodon), shellfish poisoning (neurotoxic, paralytic, amnesic), mushroom poisoning, organophosphate pesticides, thallium poisoning, Guillain-Barré syndrome associated with *Campylobacter jejuni* diarrhoea; systemic illness suggests *Listeria monocytogenes,*

Brucella, Vibrio vulnificus, Trichinella spiralis, Toxoplasma gondii, hepatitis A virus (0.8% of foodborne disease outbreaks in USA, 0.8% of cases, no deaths; incubation period 15-50 d; from shellfish, foods prepared by infected food handler); if unexplained, consider saving *Escherichia coli* for labile toxin, stable toxin, invasiveness, adherence testing and serotyping, and save stool for *Rotavirus*, and stool + paired sera for *Norovirus* testing; sigmoidoscopy in symptomatic homosexual males should distinguish proctitis in the distal 15 cm only (caused by *Simplexvirus*, gonococcal, chlamydial or syphilitic infection) from colitis (with *Campylobacter*, *Shigella*, *Clostridium difficile* or *Chlamydia* infections) or non-inflammatory diarrhoea (due to giardiasis); immunocompromised hosts should have a wide range of viral (eg., *human cytomegalovirus*, *Simplexvirus*, *coxsackievirus*, *Rotavirus*), bacterial (eg., *Salmonella*, *Mycobacterium avium-intracellulare*, *Listeria),* fungal (eg., *Candida*) and parasitic (eg., *Cryptosporidium*, *Strongyloides*, *Entamoeba histolytica* and *Giardia lamblia*) agents considered

Treatment: hydrate with oral replacement solution (child: fruit juice drinks or carbonated beverages diluted 1 in 4 with warm water) or i.v.; antibiotics should only be used for dysentery and suspected cholera; otherwise, they are ineffective and should not be given; antiparasitic drugs should only be used for amoebiasis (after antibiotic treatment of bloody diarrhoea for *Shigella* has failed or trophozoites of *Entamoeba histolytica* containing red blood cells seen in feces) and for giardiasis (when diarrhoea has lasted at least 14 d and cysts or trophozoites of *Giardia lamblia* are seen in feces or small bowel fluid); antidiarrhoeal drugs and antiemetics should never be used since none has proven practical value and some are dangerous

Epidemic Viral Diarrhoea: 80% of acute diarrhoea; incubation period 16-36 h; duration of illness 1-2 d

Agents: *Norovirus* (in 84% of infections; low infectious dose, prolonged asymptomatic shedding, environmental stability, substantial strain diversity, lack of lasting immunity; 4% of foodborne disease outbreaks in Australia; 23 M estimated cases/y in USA, 7% of foodborne related deaths, 0.3% of foodborne disease outbreaks, 1% of cases), *Rotavirus* A (mainly infants; > 9% of children worldwide infected by 3 y; causes ≈ 1/3 diarrhoea-associated hospitalisations (in Australia, ≈ 50% of those in children; rate from 9.2/1000 in Victoria to 50/1000 in Northern Territory) and 800,000 deaths/y; adult outbreaks in hospitals, nursing homes, isolated communities and travellers; 0.9% mortality), adenovirus (6% of hospitalised children with diarrhoea; 0.2% mortality in infants; types 40, 41 and others in AIDS; 15% of nosocomial), *Astrovirus* (7% of hospitalised children with diarrhoea), 3% parvovirus (in 47% of infections; 19% of water-borne outbreaks), *Sapovirus,* poliovirus 2 and 3, coxsackievirus (A, B3 probable etiologic agents), echovirus (probable etiologic agent; 7, 9, 11 (in 23% of infections), 12 (in 100% of infections), 14 and 18), measles, parainfluenza (in 15% of cases), ? *Human torovirus*, ? *Human picobirnavirus*

Diagnosis: abrupt onset, diarrhoea, abdominal pain, vomiting common, fever uncommon, upper respiratory symptoms common, convulsions rare, anal sphincter laxness rare; stools loose, more or less malodorous, blood rare, colour variable, mucus absent; no leucocytes in feces; viral culture of feces; radioimmunoassay, ELISA (antigen and antibody), agglutinations, direct immunofluorescence, electron microscopy and immune electron microscopy (research method) of feces; hemagglutination inhibition antibody technique, neutralisation antibody titre

***Rotavirus*:** from fecally contaminated foods, ready to eat foods touched by infected food workers (salads, fruits); age 6 mo - 2 y, incubation period 1-3 d, diarrhoea ++++ (75% watery), vomiting in 85%, abdominal pain in 62%, low grade fever in 28%, myalgia, headache; duration of symptoms 3-5 d; at d3-d6, 2-3 mm pink-red macules on trunk, spreading to limbs and face; no leucocytes or erythrocytes in stool micro; antigen detection by enzyme immunoassay

***Norovirus*:** adults and school-aged children, incubation period 1-2 d, nausea in 90-97% of cases, watery vomiting ++++ in 85-97%, abdominal pain and cramps ++ in 80-86%, chills in 78%, muscle aches in 67%, fever + in 64-66%, headache in 61-70%, large volume diarrhoea in 58-84%, sore throat in 10%; duration of symptoms 12-60 h; shedding from patients up to 3 w; 72% of sourced infections from food (poorly cooked shellfish, raw seafood, ready to eat foods touched by infected food workers, salads, sandwiches, ice, cookies, fruit), 22% person-to-person and 6% waterborne; no leucocytes or erythrocytes in stool micro; electron microscopy and immune electron microscopy; > 4X increase in antibody titre (enzyme immunoassay); nucleic acid hybridisation assay and reverse transcriptase-polymerase chain reaction

***Sapporo virus*:** children < 5 y; 95% diarrhoea during first 5 d, 60% vomiting on first day; shedding up to 14 d; laboratory tests as for *Norovirus*

Other Viral Agents: from faecally contaminated foods or water, ready to eat foods touched by infected food workers, some shellfish; incubation period 10-70 h; nausea, vomiting, diarrhoea, malaise, abdominal pain, headache, fever; duration of illness 2-9 d; virus isolation, serology

Treatment: rehydration, restricted diet; dehydration requires hospitalisation and fluid replacement under biochemical control

***Norovirus*:** bismuth sulphate

***Rotavirus*:** severe diarrhoea may require fluid and electrolyte replacement; infants, children, elderly and immunocompromised especially vulnerable

Prophylaxis (*Rotavirus*): tetravalent rhesus-human reassortant *Rotavirus* vaccine (49-68% protection against diarrhoea, 61-100% against severe disease) no longer recommended because of substantial increase in intussusception; live oral pentavalent vaccine also possibly linked to intussesception; hyperimmune bovine colostrum containing anti-*Rotavirus* antibodies

HAKURI (ALIMENTARY TOXICOSIS, CHOLERA INFANTUM, PSEUDOCHOLERA INFANTUM, SAKAMOTO DISEASE)

Agent: ? *Rotavirus*

Diagnosis: vomiting and diarrhoea with whitish, watery stools; low grade fever in most cases, cough in some

Treatment: rehydration, restricted diet; dehydration requires hospitalisation and fluid replacement under biochemical control; oral human gamma globulin or bovine milk concentrate containing antibody to *Rotavirus*

INFANTILE DIARRHOEA

Agents: certain serotypes of *Escherichia coli*

Diagnosis: age 0-5 y, no diarrhoea in household, gradual onset, vomiting uncommon, fever absent, convulsions rare, anal sphincter normal; stools loose, slimy, foul odour, blood rare, colour green, mucus variable; laboratory tests to identify relevant strains are grossly inadequate; serotyping against the limited range of serotypes believed to be important enteropathogenic strains is the only method suitable for routine use; complement lysis is used in research

Treatment: ampicillin or aminoglycoside in systemic infection

TRAVELLER'S DIARRHOEA (ADEN GUT, AZTEC TWO STEP, BACKDOOR SPRINT, BASRA BELLY, CANARY DISEASE, CASABLANCA CRUD, COELIAC FLUX, DEHLI BELLY, GIS, GREEK GALLOP, GYPPIE TUMMY, HONG KONG DOG, LE TURISTA, MALTA DOG, MEXICAN CALL IT, MONTEZUMA'S REVENGE, PASSION, POONAH POOHS, RANGOON RUNS, SAN FRANCISCITIS, SUMMER COMPLAINT, TOURIST TROTS, TURKEY TROTS): mild cholera-like disease in adults; incidence 3-54%

Agents: 20-62% none identified, 8-75% enterotoxigenic strains of *Escherichia coli* (744-1000 million episodes with 4-6 M deaths annually in Africa, Latin America and Asia excluding China), 0.5-2% enteroinvasive *Escherichia coli*, 0-36% *Rotavirus*, 0-30% *Shigella* (17% of notified cases in Australia), 0-25% *Salmonella* (8% of *Salmonella* notifications in Australia), 0-15% enteroadherent *Escherichia coli*, 0-15% *Campylobacter jejuni*, 0-10% *Giardia lamblia*, 0-8% *Aeromonas*, 0-7% *Vibrio parahaemolyticus* (diarrhoea in 95% of infections), 0-7% *Plesiomonas shigelloides,* 0-5% *Entamoeba histolytica*, 0-2% *Vibrio cholerae* non-01, 0-2% *Cryptosporidium*, 0-1% *Vibrio fluvialis,* 0-1% *Yersinia enterocolitica* (diarrhoea in 86% of infections), 0-1% enterohemorrhagic *Escherichia coli*, 0-0.3% *Vibrio cholerae* 01, *Vibrio vulnificus, Vibrio alginolyticus, Vibrio mimicus, Vibrio furnissii*

Diagnosis: 3-8 stools/d in 80% of cases; abdominal pain and cramps in most cases; fever, vomiting, bloody stools in 10-20%; typically lasts 3-5 d but > 1 w in 10%; micro for parasites, bacterial and viral culture of feces

Enterotoxigenic *Escherichia coli:* highest in summer; 99% diarrhoea, 79-82% abdominal pain and cramps, 49% nausea, 17-22% fever, 14-54% vomiting; from water or food contaminated with human feces; incubation period 1--3 d; duration of illness 3->7 d; 87% of cases 5-10 stools/d, 78% watery, 40% mucus, 12% blood, no leucocytes; test for toxin production in Chinese hamster ovary cells

Invasive *Escherichia coli* and Shigellosis: 78% of cases 5-10 stools/d, 60% blood, 70% mucus, 24% watery; 85% polymorphonuclears in feces

Salmonella: 75% of cases 5-10 stools/d, 50% mucus, 33% watery, 21% blood

***Campylobacter jejuni*:** highest in winter; diarrhoea in all cases; 82% explosive, watery; 66% > 10 stools/d; 26% with blood, 61% mucus; 8% persisting or recurring 2 w or more

***Aeromonas*:** 56% of cases 5-10 stools/d, 51% watery, 37% mucus, 15% blood, 33% guiac test positive, 50% diarrhoea 3-10 d, 50% > 10 d

***Cryptosporidium*:** from contaminated water, vegetables, fruits, unpasteurised milk, swimming pools; incubation period 2-28 d; diarrhoea in 84% of infections (5-10 watery, frothy bowel movements/d), cramping, abdominal pain, sometimes fever, vomiting; usually lasting 1-5 d in noncompromised and months in compromised

***Vibrio cholerae* 01:** bloody, watery

Vibrio vulnificus: vomiting, diarrhoea, abdominal pain, bacteremia, may be wound infections; more common in immunocompromised and patients with chronic liver disease (associated bullous skin lesions); incubation period 1-7 d; duration of illness 2-8 d; from undercooked or raw shellfish (especially oysters), other contaminated seafood (also open wounds exposed to sea water); stool cultures on thiosulphate citrate bile sucrose agar; wound and blood cultures if indicated

Vibrio parahaemolyticus: acute watery diarrhoea, abdominal cramps, nausea, vomiting; incubation period 2-48 h; from undercooked or raw seafood (especially shellfish); stool culture on thiosulphate citrate bile sucrose agar

Vibrio fluvialis: diarrhoea in 100% (75% bloody), vomiting in 97%, abdominal pain in 75%, dehydration in 67%, fever in 35%

Treatment:

Mild (1-2 Loose Stools/24h, Tolerable Symptoms): rehydration, dietary restriction

Moderate to Severe: azithromycin 20 mg/kg to 1 g orally as single dose or norfloxacin 20 mg/kg to 800 mg orally as single dose; if no improvement of if fever or bloody stools, azithromycin 10 mg/kg to 500 mg orally daily for 2-3 d or norfloxacin 10 mg/kg to 400 mg orally 12 hourly for 2-3 d or ciprofloxacin 10 mg/kg to 500 mg orally 12 hourly fo 2-3 d

Persistent (> 3 w) and No Clear Diagnosis: tinidazole 2 g orally with food as a single dose

Prophylaxis:

High Risk Host (Immunodeficiency Including AIDS, Insulin Dependent Diabetes Mellitus, Active Inflammatory Bowel Disease, Cardiac or Renal Failure, Use of Potent H_2-receptor Antagonists or Omeprazole): norfloxacin 10 mg/kg to 400 mg orally daily or ciprofloxacin 10 mg/kg to 500 mg orally daily for not more than 3 w

Purpose of Trip Would be Ruined by Illness: colloidal bismuth subcitrate 2 tablets chewed with meals and at bedtime to 8 tablets/d for not more than 3 w

consumption of beverages ready bottled or heated and of food immediately after cooking; avoidance of unpasteurised milk and fruits and salads washed in suspect water; disinfection of water by boiling or chlorination

AMOEBIASIS (AMEBIASIS, AMOEBOSIS, ENTAMOEBIASIS): global mortality 40,000-110,000/y, global morbidity 35-50 M; transmitted by cysts of carriers; invasive infection in ≈ 10% of symptomatic cases, extraintestinal amobeiasis in ≈ 5%

Agents: *Entamoeba histolytica*; *Entamoeba polecki* in Australian Aborigines and Papua New Guineans, also S E Asian refugees

Diagnosis: dependent on presentation; ELISA superior to indirect haemagglutination assay in diagnosis of extraintestinal amoebiasis and helps in detecting *Entamoeba histolytica* in otherwise undiagnosed hepatomegaly

Treatment:

Intestinal: see below

Extraintestinal: metronidazole 750 mg 3 times a day for 5-10 d + iodoquinol 650 mg 3 times a day for 20 d; dehydroemetine 1 mg/kg/d to maximum 90 mg/d s.c. or i.m. for 5 d + chloroquine phosphate 600 mg base daily for 2 d then 300 mg base daily for 2-3 w

INTESTINAL AMOEBIASIS: incubation period 2 d - 4 w; duration of illness months; fecal-oral transmission and may contaminate water and food; 1% of infective diarrhoea in adults; may be either noninvasive or invasive; carrier state occurs in noninvasive intestinal amoebiasis or may follow any invasive stage; chronic intestinal amoebiasis (chronic amoebic colitis, chronic amoebiasis, chronic amoebic dysentery) has been described

Agent: *Entamoeba histolytica*

Diagnosis:

Noninvasive Intestinal Amoebiasis: as a rule, asymptomatic; no hematophagous trophozoites, changes observable at endoscopy or specific antibodies

Invasive Intestinal Amoebiasis: intermittent diarrhoea, acute dysentery with bloody, mucous stools, colicky pain and rectal tenesmus; may be weight loss and dehydration, fever, constipation, headache, drowsiness, colonic lesions and perforations; incubation period 1 to several weeks

Fulminating Amoebic Colitis: severe form characterised by passage of numerous bloody stools, generalised abdominal discomfort, colicky pains preceding evacuation and rectal tenesmus (often constant and intense), with fever, dehydration and prostration; may be intestinal hemorrhage or perforation

Amoeboma (Amoebic Granuloma): granulomatous tumour-like mass that occasionally develops on intestinal wall

Other Complications: megacolon, peritonitis, amoebic appendicitis and cecitis, cutaneous amoebiasis, rectovaginal amoebic cuffs, hemorrhage, rectovesicular fistulas; acute necrotising colitis with toxic megacolon in 0.5% (associated with > 40% of deaths)

geographic history; incubation period < 21 d; 97% of stools with macroscopic mucus, 37% with macroscopic and 57% with microscopic blood (often in rouleaux), 98% with leucocytes (59% > 10/hpf, variable numbers of mononuclears), 74% pH alkaline; microscopic examination of fresh, warm, liquid feces for hematophagous trophozoites; merthiolate iodine formalin concentration and staining of multiple stool specimens, concentrated by modified Ritchie formalin-ether, and examined stained (iron hematoxylin, trichrome) and as wet mounts for trophozoites and cysts (sensitivity 30-50%, specificity < 60%); sigmoidoscopic swabs and scrapings from large bowel ulcers and biopsies of rectal mucosa; culture adds little in the way of sensitivity or precision to microscopic methods; indirect hemagglutination (10% asymptomatic cyst carriers, < 50% amoebic diarrhoea, 85% invasive amoebic dysentery, > 90% amoebic abscess = 256), counterimmunoelectrophoresis, complement fixation test (diagnostic titre 1:4), latex agglutination, immunodiffusion, ELISA (antigen; stool, sensitivity > 95%, specificity >95%; serum sensitivity > 65%, specificity 90%; salivary IgA diagnostic accuracy 91.5%); indirect immunofluorescence with monoclonal antibodies distinguishes pathogenic (*E.histolytica*) from nonpathogenic (*E.dispar*) strains; negative tests do not exclude intestinal amoebiasis; active infection indicated by presence of specific IgM and IgG; culture and isoenzyme analysis (sensitivity 30-60%, 100% specificity; requires 1-2 w); PCR on stool (sensitivity > 85%, specificity > 90%); colonoscopy; anemia (erythrocyte count and hemoglobin decreased)

Differential Diagnosis:

Dysentery: infections due to *Shigella*, *Campylobacter jejuni*, *Yersinia enterocolitica*, invasive *Escherichia coli*, *Vibrio parahaemolyticus*

Mild Diarrhoea Syndrome: *Salmonella*, giardiasis, enterotoxigenic *Escherichia coli* diarrhoea, many other diarrhoeas of infectious origin, irritable bowel syndrome

Treatment:

Cyst Passers: diloxanide furoate 500 mg orally 3 times daily (child: 20 mg/kg/d in 3 divided doses) for 10 d, iodoquinol 650 mg 3 times daily (child: 30-40 mg/kg/d to 2 g in 3 doses) for 20 d, paromomycin 25-30 mg/kg/d in 3 divided doses for 7 d

Symptomatic: tinidazole 50 mg/kg to 2 g orally daily for 3 d or metronidazole 15 mg/kg to 600 mg orally 8 hourly for 7-10 d, followed by diloxanide furoate 7 mg/kg to 500 mg orally 8 hourly for 10 d or paromomycin 10 mg/kg to 500 mg orally 8 hourly for 7 d or iodoquinol 650 mg 3 times daily for 20 d

Prevention and Control: sanitation, control of carriers

Bacillary (Bacterial) Dysentery (Shigellosis and Coliform Enteritis)

Shigellosis: ≈ 500 notified cases/y in Australia (≈ 24% in Queensland); incidence in USA 8/100,000 in general population and 494/100,000 in Indian reservations (450,000 estimated total cases, 20% foodborne, 0.8% of foodborne related deaths; 2% of foodborne disease outbreaks, 2% of cases); 2% of infectious diarrhoea (7% in adults; 15% of bloody diarrhoea); transmission by contaminated water and food (usually person-to-person fecal-oral route through ready to eat foods touched by infected workers, raw vegetables, egg salads); duration of illness 4-7 d; case-fatality rate 0.06%; increased risk in men who have sex with men

Agents: *Shigella sonnei* (group D shigellosis, Sonne dysentery; 93% of cases in institutions, 74% in general population, 41% in Indian reservations; very mild infection), *Shigella flexneri* (Flexner dysentery, group B shigellosis, Hiss-Russel dysentery; 7% of cases in institutions, 23% in general population, 58% in Indian reservations), *Shigella boydii* (Boyd dysentery, group C shigellosis; 2-3% of cases), *Shigella dysenteriae* (group A shigellosis, Shiga-Kruse dysentery; serotype 1: Shiga dysentery; serotype 2: Schnitz dysentery; tropics; more serious; 1% of cases), enteroinvasive strains of *Escherichia coli* (≈ 40 notified cases/y in Australia)

Diagnosis: incubation period 12 h - 7 d (usually 24-48 h) in shigellosis, 1-18 h in enteroinvasive *Escherichia coli*; severe diarrhoea, abdominal pain and cramps in 82% of *Shigella* and 91% of enteroinvasive *Escherichia coli*, moderate fever in 40-42% of *Shigella* and 40% of enteroinvasive *Escherichia coli*, slight vomiting in 66% of *Shigella* and 73% of enteroinvasive *Escherichia coli*, age 6 mo - 6 y (rare in neonates), > 50% diarrhoea in household, onset abrupt, bronchitis common, convulsions common, anal sphincter lax tone (rarely rectal prolapse); feces watery and consists largely of mucus (macroscopic in 66-94% of *Shigella* and 66% of enteroinvasive

Escherichia coli) and blood (macroscopic in 37-63% of *Shigella* and 18% of enteroinvasive *Escherichia coli* and microscopic in 75% of cases), relatively odourless, yellow-green (almost colourless in severe cases) and contains large numbers of neutrophils (in 99% of cases; 44-80% > 10/hpf; 85% of leucocytes) and erythrocytes (18-43% > 10/hpf; scattered), large macrophages may be present and may have ingested red cells, pH alkaline in 68% of cases; diffuse colitis by sigmoidoscopy; micro, culture (Gram negative broth, xylose lysine deoxycholate agar, MacConkey) and immunofluorescent staining of feces or rectal swab; presence of toxin confirmed by DNA hybridisation and ELISA test; neutrophilia in blood smear; anemia (erythrocyte count and hemoglobin decreased); no satisfactory routine test for identification of *Escherichia coli* strains

Treatment: supportive; antibiotics recommended in all cases for public health reasons; norfloxacin 10 mg/kg to 400 mg orally 12 hourly for 5d (contraindicated in children), cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly for 5 d, ampicillin 25 mg/kg to 1 g orally 6 hourly for 5 d; in severely ill or immunocompromised, ciprofloxacin 10 mg/kg to 500 mg orally 12 hourly for 5 d; zinc 20 mg/d for 2 w

Prevention and Control: identification and enteric isolation of cases; good hygiene

Cholera (Algid Cholera, Asiatic Cholera, Asphyctic Cholera, Cholera Gravis, Cholera Indica, Cholera Orientalis, Cholera Sicca, Cholera Siderans, Dry Cholera, Epidemic Cholera, Indian Cholera, Malignant Cholera, Pandemic Cholera, Spasmodic Cholera): illness characterised by diarrhoea and/or vomiting; severity is variable; transmission by contaminated water, fish, shellfish, street-vended food; incubation period 24-72 h; duration of illness 3-7 d; principally Africa, Arab countries, India, Indonesia, S America but becoming widespread over Indo-Pacific; few sporadic indigenous cases in Australia (≈ 3 notified cases/y); indigenous focus of infection in crustaceans in Gulf of Maine in USA; incidence in USA 0.3/100,000; global incidence 384,000/y; global mortality 20,000/y; death due to dehydration produced by excess water secretion into small intestine in response to increased activity of adenyl cyclase stimulated by exotoxin of organism; case-fatality rate 0.7%

Agent: *Vibrio cholerae* 01 biotype cholerae (classical cholera; infection:case ratio 5:1-10:1) and biotype eltor (cholera el Tor, cholera El Tor, cholera el tor, cholera eltor; infection:case ratio 25:1-100:1)

Diagnosis: 75% asymptomatic, 18% mild, 5% moderate, 2% severe; abrupt onset of profuse watery diarrhoea; 58% > 10 stools/d, 88% watery, 8% mucus, 4% blood; explosive), occasional vomiting, fever absent, respiratory symptoms absent, occasional convulsions, anal sphincter normal, saline depletion, hypotension; stools innocuous odour, clear, rice water; geographic history; micro (leucocytes absent; organisms seen in Gram or on phase or dark field) and culture of feces or vomit on thiosulphate citrate bile sucrose medium (enrichment in alkaline peptone water will increase yield), with isolation of cholera toxin-producing *Vibrio cholerae* 01 or 0139 (confirmed by DNA hybridisation and ELISA test); serologic evidence of recent infection (ELISA; sensitivity 85-100%)

Treatment: rehydration and electrolyte replacement (severe dehydration: i.v. Ringer's lactate; less severe: oral rehydration with sodium chloride 3.5 g/L + sodium citrate dihydrate 2.9 g/L or sodium bicarbonate 2.5 g/L + potassium chloride 1.5 g/L + anhydrous glucose 20 g/L + zinc 40 mg/L in clean drinking water); antibiotics reduce volume and duration of diarrhoea; doxycycline 2.5 mg to 100 mg orally 12 hourly for 3 d (not in < 8 y, pregnant or breastfeeding), ciprofloxacin 25 mg/kg to 1 g orally single dose (not pregnant or children), norfloxacin 400 mg twice a day for 3 d (not pregnant or children), tetracycline 30-40 mg/kg to 500 mg orally 6 hourly for 3 d (not in < 8 y, pregnant or breastfeeding), erythromycin 250 mg orally 4 times daily (child: 10 mg/kg 3 times daily) for 3 d, azithromycin 20 mg/kg single dose, cotrimoxazole

Pregnant, < 8 y: amoxycillin 10 mg/kg to 250 mg orally 6 hourly for 5 d

Carriers: oral streptomycin or neomycin

Prophylaxis: no vaccine currently licensed and available; 'boil it, cook it, peel it or forget it'; improved sanitation; postexposure: doxycycline 2 mg/kg to 100 mg orally daily

Enterotoxemia: preformed toxin in food

Agents: *Staphylococcus aureus* (185,000 estimated cases/y in USA, all foodborne, 0.1% of foodborne related deaths; 2% of foodborne outbreaks, 2% of cases; heat-stable toxin in unrefrigerated or improperly refrigerated cream pastries, meats, potato and egg salads; duration of illness 24-48 h), *Clostridium perfringens* type A (heat-stable toxin in meats, poultry, gravy, dried or precooked foods kept warm for several hours; duration of illness 24-48 h; 18% of foodborne disease outbreaks in Australia; 250,000 estimated cases/y in USA, all foodborne, 0.4% of foodborne related deaths; 2% of foodborne disease outbreaks, 3% of cases), *Clostridium botulinum* (8-66% mortality; heat-labile toxin in home-canned foods with low acid content, improperly canned commercial foods, home-canned or fermented fish, herb-infused oils, baked potatoes in aluminium foil, cheese sauce, bottled garlic, foods held

warm for extended periods; no notified cases in Australia in past decade), *Bacillus cereus* (diarrhoeal toxin from meats, stews, gravies, vanilla sauce; vomiting toxin from improperly refrigerated cooked and fried rice, meats; 27,000 estimated cases/y in USA, all food borne, no deaths; 0.5% of foodborne disease outbreaks, 0.8% of cases)
Diagnosis: isolation of organism from suspect food (chopped meat, blood agar, phenylethyl alcohol blood agar, mannitol salt agar, tryptose sulphite cycloserine agar) and feces; identification of toxin (ELISA) from feces, serum (≈ 3-5 mL transported at 4ºC) and foodstuff; CSF pressure, cell count, glucose and protein normal

***Staphylococcus aureus*:** sudden onset of very severe nausea, retching and vomiting and abdominal pain and cramps, slight diarrhoea in 39% of cases, little or no fever, acute prostration; incubation period 0.5-6 h

Clostridium perfringens: very severe abdominal pain and cramps, moderate watery diarrhoea in 91% of cases, vomiting rare, little or no fever, nausea and headache rare; incubation period 8-16 h; toxin test on stool

Clostridium botulinum: moderate bulbar signs, vertigo, double or blurred vision, loss of reflex to light, difficulty in swallowing, speaking and breathing, dry mouth, descending muscle weakness, respiratory paralysis; slight vomiting, diarrhoea in some cases; incubation period 2 h - 8 d; duration of illness days to months; toxin test on stool, serum and food

***Bacillus cereus*:** diarrhoeal toxin: abdominal cramps, nausea, watery diarrhoea, incubation period 10-16 h, duration of illness 24-48 h; vomiting toxin: sudden onset of nausea and vomiting ± diarrhoea, incubation period 1-6 h, duration of illness 24 h; test food and stool for toxins in outbreaks
Treatment: supportive

***Clostridium botulinum*:** antitoxin
Prophylaxis (Botulism): hyperimmune immunoglobulin
CIGUATERA FISH POISONING: pantropical; 13% of foodborne disease outbreaks in Australia; 2% of foodborne disease outbreaks in USA, 0.2% of cases, no deaths
Agent: ciguatoxin and 5 other toxins produced by *Gambierdiscus toxicus* (a diatom) eaten by fish (coral reef fish, barracuda, grouper, amberjack, red snapper), which concentrate toxin and remain toxic 2 y
Diagnosis: clinical: gastrointestinal symptoms (abdominal pain, nausea, vomiting, diarrhoea) 2-6 h post-ingestion, neurologic (paresthesias of lips, tongue and extremities, reversal of hot and cold, pain and weakness of lower extremities, acral tingling, myalgia, itching, insomnia, headache, numbness and aching teeth usually present; dizziness, dry mouth, dilated pupils, blurred vision, paralysis, seizures, coma and death (rarely) also occur) 3 h post-ingestion, cardiovascular (bradycardia, hypotension, increase in T wave abnormalities) after 2-5 d; duration of illness days to months; radioassay for toxin in suspect fish
Treatment: supportive, i.v. mannitol, tocanide, amitryptyline (25 mg twice a day), nifedipine
NEUROTOXIC SHELLFISH POISONING: Caribbean, Gulf of Mexico
Agent: ≥ 10 brevetoxins produced by *Karenia brevis* and concentrated by shellfish; most common in US Gulf States; marine mammal deaths
Diagnosis: clinical (incubation period 2 min-4 h; reversal of hot and cold sensation, nausea, vomiting, diarrhoea, tingling and numbness of lips, mouth, tongue, throat and face, muscle aches, dizziness, ataxia, asthma-like respiratory distress, often a feeling of floating); history of shellfish (mussels, plankton feeders) ingestion; detection of toxin in shellfish
Treatment: supportive; activated charcoal and cathartic if severe
PARALYTIC SHELLFISH POISONING: subarctic to tropic (primarily American Samoa, California, Washington, New England
Agent: saxitoxin (blocks sodium channels) and ≥ 21 other toxins produced by *Gonyaulax* and *Alexandrium* and concentrated by finfish and shellfish
Diagnosis: clinical (incubation period 30 min to 3 h; diarrhoea, nausea, vomiting, abdominal pain, paresthesias of extremities, tingling, burning, numbness of mouth and lips, drowsiness, incoherent speech, ataxia (rare), respiratory paralysis (rare), death (rare)); history of shellfish (mussels, clams, scallops, cockles) ingestion; duration of illness days; detection of toxin in food or water where fish located
Treatment: supportive; activated charcoal and cathartic if severe; may be life-threatening and need respiratory support
DIARRHOEIC SHELLFISH POISONING: Europe, Canada, Japan, New Zealand, South America, seen in US waters
Agent: dinophysis toxin, okadaic acid, pectenotoxin, yessotoxin produced by *Dinophysis*

Diagnosis: ingestion of a variety of shellfish, primarily mussels, oysters, scallops, shellfish from Florida coast and Gulf of Mexico; incubation period 30 min to 2 h; abdominal pain, vomiting, nausea, headache, diarrhoea, chills, fever; duration of illness hours to 3 d; demonstration of toxin in shellfish
Treatment: supportive
SCOMBROID POISONING: 4% of foodborne disease outbreaks in Australia; 3% of foodborne disease outbreaks in USA, 0.3% of cases, no deaths
Agent: histamine produced by bacterial action on flesh of certain fish (tuna, mackerel, mahi-mahi, bonito, bluefin, skipjack, marlin)
Diagnosis: incubation period 1 min-3 h; dizziness, headache, respiratory symptoms, nausea, vomiting, peppery taste, burning of mouth, throat and skin, facial swelling and flushing, stomach pain, itching of skin, rash, urticaria, paresthesias; duration of illness 3-6 h; demonstration of histamine in food
Treatment: gastric lavage, antihistamine, cimetidine, bronchodilators if wheezing or asthmatic
TETRODOXIN POISONING: kills 70-100/y in Japan
Agent: tetrodoxin from blowfish (puffer, globefish, swellfish, fugu)
Diagnosis: tingling about lips and tongue and feeling as though floating, followed by motor incoordination within 10-45 min, then paralysis, difficulty swallowing and loss of voice; death due to respiratory paralysis in > 60%
AMNESIC SHELLFISH POISONING: Canada, NE USA, Washington, Oregon, California
Agent: domoic acid produced by *Pseudo-nitzchia pungens* and other species and concentrated by shellfish (especially mussels) and finfish
Diagnosis: gastroenteritis, memory defects/amnesia, confusion, death (4%)
Treatment: supportive
INFANT BOTULISM: in infants < 12 mo; associated with honey, home-canned vegetables and fruits, infant formula
Agent: *Clostridium botulinum*
Diagnosis: incubation period 3-30 d; duration of illness variable; weakness or floppiness in 88%, poor feeding in 79%, constipation in 65%, weak cry in 18%, irritability in 18%, respiratory difficulties in 11%, seizures in 2%; electromyogram (compound muscle action potentials of decreased amplitude in at least 2 muscle groups; tetanic and post-tetanic facilitations defined by an amplitude of > 120% of baseline; prolonged post-tetanic facilitation of > 120 s and absence of post-tetanic exhaustion); toxin identification (mouse bioassay, ELISA) from stool (25-50 g without transport medium transported at 4^{0}C), serum, food; recovery of *Clostridium botulinum* from stool and suspect materials
Treatment: supportive; botulism immune globulin
BACTERIAL GASTROENTERITIS (BACTERIAL ENTERITIS): although toxins may be produced and play a role in disease causation, the condition arises from a true infection and is not only an intoxication; most common cause (14%) of fever in returned travellers to Australia
Agents: *Salmonella* (≈ 7000 notified cases/y in Australia (≈ 31% in Queensland), 46% of foodborne disease outbreaks; incidence 12/100,000 in USA (1.4 M estimated total cases, 95% foodborne, 31% of foodborne related deaths; 13% of foodborne disease outbreaks, 38% of cases); 34% of infectious diarrhoea in adults; 6% of bloody diarrhoea; mortality < 1%; infection from contaminated eggs, poultry, fish, ham, beef, gravy, meat pies, sausages, raw fruits and vegetables, unpasteurised milk or juice, soft cheese or fecal contamination; duration of illness 4-7 d), *Yersinia enterocolitica* (2% of infectious diarrhoea; ≈ 140 notified cases/y in Australia (general decline; ≈ 70% in Queensland); incidence 0.5/100,000 in USA (100,000 estimated total cases, 90% foodborne, 0.1% of foodborne related deaths); vehicle contaminated water and unpasteurised milk, juice or soft cheeses in outbreaks, undercooked pork in sporadic cases), *Plesiomonas shigelloides* (1% of infectious diarrhoea in adults; occasional bloody diarrhoea; occasional outbreaks and sporadic cases, chiefly in tropical areas), *Vibrio parahaemolyticus* (0.7% of infectious diarrhoea in adults; from fish, shellfish and processed seafood; duration of illness 24-72 h), *Aeromonas hydrophila* (0.7% of infectious diarrhoea in adults), enterotoxigenic (undercooked hamburger, unpasteurised juices) and enteropathogenic adhesion factor positive *Escherichia coli* (dyspepsiacoli diarrhoea, *Escherichia coli* diarrhoea; < 1% of infectious diarrhoea; > 10^{6} bacteria in food or water), *Clostridium perfringens* (uncommon), *Vibrio cholerae* non-01, *Vibrio mimicus, Vibrio fluvialis, Vibrio furnissi, Vibrio hollisae* and *Vibrio vulnificus* (vehicle shellfish), *Listeria monocytogenes* (usually milk products (unpasteurised soft cheeses); also raw hot dogs, deli meats; ≈ 60 notified cases/y in Australia, 4% of foodborne disease outbreaks; incidence 0.4/100,000 in USA (3000

estimated total cases, 99% foodborne, 28% of foodborne related deaths; 0.1% of foodborne disease outbreaks, 0.1% of cases)), rarely *Enterococcus faecalis, Enterococcus faecium, Proteus, Alcaligenes faecalis, Pseudomonas aeruginosa* ('Shangai fever'; presentation similar to typhoid fever), *Edwardsiella tarda*

Diagnosis: micro (leucocytes (75% polymorphonuclears) but usually not erythrocytes) and culture (blood agar, enteric and differential agar media) of feces; ELISA for antibody (*Salmonella enteritidis* sensitivity 92%, specificity 100%; *Salmonella typhimurium* sensitivity 100%; *Yersinia enterocolitica* sensitivity 86%, specificity 100%); toxin assay (*Clostridium perfringens*)

Salmonella: moderate vomiting in 56%, diarrhoea, abdominal pain and cramps in 75%, variable fever in 27%, chills, malaise, nausea, headache, prostration, respiratory symptoms uncommon, convulsions rare, anal sphincter normal; stools loose, slimy, foul odour (rotten eggs), blood in 26%, colour green, mucus variable; incubation period 1-3 d; TUBEX detects IgM antibodies to *Salmonella enteritidis* (sensitivity 93%, specificity 95%)

Vibrio parahaemolyticus: nausea and vomiting, severe abdominal pain and acute watery diarrhoea; incubation period 2-48 h

Vibrio vulnificus: vomiting, diarrhoea, abdominal pain, bacteremia, may be wound infections; more common in immunocompromised and patients with chronic liver disease (associated bullous skin lesions); incubation period 1-7 d; duration of illness 2-8 d; from undercooked or raw shellfish (especially oysters), other contaminated seafood (also open wounds exposed to sea water); stool cultures on thiosulphate citrate bile sucrose agar; wound and blood cultures if indicated

Yersinia enterocolitica: diarrhoea, vomiting, fever, abdominal pain; appendicitis-like symptoms primarily in older children and young adults; incubation period 24-48 h; duration of illness 1-3 w; occasionally bloody diarrhoea; culture of stool or vomitus on CIN medium; blood culture; serology (research and reference laboratories)

Enterotoxigenic *Escherichia coli*: 99% diarrhoea, 79-82% abdominal pain and cramps, 73% watery stool, 49% nausea, 17-22% fever, 14-54% vomiting; 10% severe hemorrhagic colitis; median incubation period 42 h (72-120 h); duration of illness 24-265 h; 87% of cases 5-10 stools/d, 78% watery, 40% mucus, 12% blood, no leucocytes; test for toxin production in Chinese hamster ovary cells

Enteropathogenic adhesion factor positive *Escherichia coli*: 81% watery stool, 69% vomiting, 44% abdominal pain, 19% fever; incubation period 12-74 h

Treatment: antibiotics are not usually required and, especially in salmonellosis, prolong carriage, as do agents (eg., Lomotil™) decreasing intestinal motility; patients with AIDS or lymphadenopathic syndrome, oncology patients and, possibly, patients > 50 y, infants < 3 mo and malnourished children should, however, receive antibiotic treatment, as should systemic infections; dehydration requires hospitalisation and fluid replacement under biochemical control

Salmonella: ciprofloxacin 10 mg/kg to 500 mg orally 12 hourly for 5-7 d, azithromycin 20 mg/kg to 1 g orally on first d then 10 mg/kg to 500 mg daily for further 6 d; if oral therapy cannot be tolerated, ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly until oral ciprofloxacin can be tolerated, ceftriaxone 50 mg/kg to 2 g i.v. daily until oral ciprofloxacin or azithromycin can be tolerated

***Yersinia enterocolitica* (Severe Cases):** gentamicin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly, cefotaxime, ceftriaxone, ciprofloxacin, doxycycline

***Vibrio parahaemolyticus* (Severe Cases):** tetracycline, doxycycline, gentamicin, cefotaxime

Vibrio vulnificus: supportive care + tetracycline, doxycycline or ceftazidime

Aeromonas: chloramphenicol, ciprofloxacin, aminoglycosides, third generation cephalosporins, aztreonam, imipenem

Plesiomonas shigelloides: chloramphenicol, aminoglycosides, cotrimoxazole, fluoroquinolones, tetracycline, third generation cephalosporins, imipenem

Listeria monocytogenes: ampicillin, cotrimoxazole

Enterotoxigenic *Escherichia coli:* cotrimoxazole

Enteropathogenic *Escherichia coli:* ampicillin, cotrimoxazole

Enteroinvasive *Escherichia coli* (Severe Cases): quinolones

GASTROENTERITIS also occurs with infections with *Taenia saginata, Taenia solium, Trichinella spiralis,* on ingestion of ciguatera toxin, tetraodon toxin and *Muscaria*-type mushrooms and in organic phosphate poisoning. Gastrointestinal distress is common in influenza and occurs in 15% of parainfluenza cases. Gastrointestinal

hemorrhage is extensive in Ebola hemorrhagic fever and occurs in neonatal *Simplexvirus* infection and in 13% of cases of brucellosis. Gastrointestinal symptoms are also seen in 94% of cases of toxic shock syndrome.

ENTERIC FEVER (EBERTH DISEASE): acute febrile disease; transmission by contact, water or food; epidemics often related to fecal contamination of water supplies or street-vended foods; may take numerous clinical forms; 80% in Asia, 20% in Latin America, Africa; global incidence 16M/y (600,000 deaths/y)

Agents: *Salmonella typhi* (typhoid fever, continued fever, febris typhoidea, ileotyphus, lent fever, nightsoil fever, pythogenic fever, typhoenteritis, typhogastric fever, typhus abdominalis; prevalent in Africa, Asia (13 M cases and > 440,000 deaths/y) and Mediterranean basin; causes epidemics anywhere; 0.4% of infectious diarrhoea; ≈ 70 notified cases/y in Australia (≈ 53% in NSW; causes 3% of fever in returned travellers); incidence 0.2/100,000 in USA; case-fatality rate 0.1-41%; perforation (case-fatality rate 0-100%) in 0-21% of cases), *Salmonella paratyphi A* (febris paratyphoidea A, paratyphoid A fever, paratyphoid fever A, paratyphus A; largely confined to tropics but also other Asia, Western Europe), *Salmonella enterica subsp Salmonella enteric I* serovar paratyphi B (Brion-Kayser disease, febris paratyphoidea B, paratyphoid B fever, paratyphoid fever B, paratyphus B, Schottmüeller disease; Europe), *Salmonella enterica subsp Salmonella enteric I* serovar paratyphi c (febris partyphoidea C, paratyphoid C fever, paratyphoid fever C, paratyphus C)

Diagnosis: gradual onset (incubation period 7-28 d), prolonged fever (≥ 39°C in 90%), malaise, headache, nausea, constipation, abdominal pain, chills, myalgia, rose spots, splenomegaly, hepatomegaly, diarrhoea and vomiting uncommon, nonproductive cough common, occasional convulsions, anal sphincter normal; stools foul odour, brown; 49% of cases with 10 stools/d, lasting 6+ d, 98% watery, 7% bloody, 2% soft, 29% guiac test positive, 52% 1-9 erythrocytes/hpf, 74% 0-19 leucocytes/hpf, 4950 leucocytes/µL, 70% polymorphs, 30% mononuclears, protein 9.3 g/L, sodium 47 mEq/L, potassium 48 mEq/L, chloride 43 mEq/l, pH 6.1; history of foreign travel, especially Mexico and India; blood culture X2 + bone marrow culture (most reliable single method) + duodenal string culture; hypochromic anemia (erythrocyte count and hemoglobin decreased), neutropenia or neutrophilia; serum alkaline phosphatase 30 IU/L, serum bilirubin 2 mg/dL, serum glutamic pyruvic acid transaminase 16-170 U/mL in 35% of cases, serum CO_2 24 mmol/L; elevated antibody titres to hemagglutinin; Widal test (agglutinins to O antigens of groups A, B, C or D or H antigen elevated in infections; cross-reactions between groups B, C and D common; high H titre in prior immunisation); radioimmunoassay (sensitivity 94%, specificity 100%)

Treatment: ciprofloxacin 15 mg/kg to 500 mg orally or 10 mg/kg to 400 mg i.v. 12 hourly for 7-10 d; if reduced susceptibility to quinolones or fever > 7 d, ceftriaxone 50 mg/kg to 2 g i.v. once daily or azithromycin 20 mg/kg to 1 g i.v. or orally daily till clinical response, then amoxicillin 25 mg/kg to 1 g orally 6 hourly for further 14 d, azithromycin 20 mg/kg to 1 g orally daily for total 10 d or cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly for 14 d; + dexamethasone 3 mg/kg in critically ill patients in shock; + aggressive resuscitation, prompt operative intervention and careful postoperative attention to hydration and nutrition in perforation

Carriers: norfloxacin 400 mg orally 12 hourly for 28 d, ciprofloxacin 750 mg orally twice daily for 28 d, ofloxacin; amoxycillin 50-75 mg/kg daily in 3 divided doses orally or i.v. + probenecid 30 mg/kg (child: 10-15 mg/kg) orally daily in divided doses for 6 w

Prophylaxis (*Salmonella typhi*): heat-killed whole cell vaccine (protection rate 70-90%; contraindicated in pregnancy and convalescence from serious illness); Vi conjugate vaccine (71-88% efficacy after single dose, 92% after 2 doses; lower fever and systemic adverse effects); live oral vaccine (protection rate 70-95%; contraindicated in pregnancy, acute gastrointestinal infections, AIDS, treatment with antimitotic or immunosuppressive drugs); good sanitation

DIARRHOEA RELATED TO BACTERIAL OVERGROWTH

Agents: mixed bacterial species in high numbers

Diagnosis: chronic diarrhoea; culture of duodenal aspirate; glucose ingestion hydrogen breath test

Treatment: norfloxacin 800 mg/d for 7 d, amoxycillin-clavulanate 1500 mg/d for 7d, rifaximin 1600 mg/d

ENTERITIS: 0.2% of new episodes of illness in UK

Agents: *Giardia lamblia* (2 M estimated cases/y in USA (10% foodborne, 0.1% of foodborne related deaths); 1% of infective diarrhoea in adults; swallowing water while swimming, recreational fresh water contact, drinking treated tap water, eating lettuce), *Chilomastix mesnili, Cystoisospora belli* (probably worldwide infection of mammals; frequently asymptomatic infection of workers in contact with farm animals, usually pigs; frequent cause (15% in Haiti) of severe diarrhoea in AIDS), *Sarcocystis, Cryptosporidium* (worldwide in most mammals; incidence

varies widely from 2.4/100,000 in USA (300,000 estimated total cases (10% foodborne), 0.4% foodborne related deaths) to 9.2% in parts of Africa), *Cyclospora cayetanensis* (Americas, Africa, Indian subcontinent, South-east Asia; incidence 0.1/100,000 in USA (16,000 estimated total cases, 90% foodborne, no deaths); transmitted in contaminated water, berries, lettuce, basil, salad), *Blastocystis hominis* (claimed to cause an acute enteritis but probably rarely, if ever, a human pathogen), *Encephalitozoon cuniculi, Enterocytozoon bieneusi* and *Encephalitozoon intestinalis* (chronic diarrhoea in AIDS), *Nosema* (immunocompromised), *Microsporidium* (immunocompromised), *Balantidium coli* (balantidiasis, balantidial colitis, balantidial dysentery, balantidiosis, balantidosis, ciliary dysentery, ciliate dysentery; worldwide; derived from pigs' feces), *Schistosoma japonicum, Schistosoma mansoni, Fasciola hepatica, Fasciolopsis buski, Dicrocoelium dendriticum, Dicrocoelium hospes, Paragonimus westermani, Nanophyetus salmincola* (10 cases in USA from eating raw, smoked or incompletely cooked salmon or steelhead trout), *Skrjabinophytus neomidis* (endemic in Siberia; infection rates up to 98%), *Opisthorchis, Clonorchis sinensis* (Southeast Asia; incidence 28M/y; no deaths reported), *Heterophyes, Metagonimus, Taenia saginata* (beef tapeworm), *Taenia solium* (pork tapeworm; cysticerci ingested in inadequately cooked pork; adult worm in intestines; eggs in feces), *Echinococcus granulosus* and *Echinococcus multilocularis* (hydatid disease; 15 cases/y in Australia), *Hymenolepis diminuta, Hymenolepis nana, Dipylidium caninum, Diphyllobothrium* (fish tapeworm; foci in Finland, Japan, Romania, Switzerland and Northern USSR; also found in Canada and Alaska in USA), *Trichinella spiralis* (incidence 0.06/100,000 in USA; attack rate 81%; case-fatality rate 9-10/1000; prevalence in USA 2%; farm-raised hogs 1/1000, garbage-fed hogs 5/1000; transmission by raw or undercooked infected meat (usually pork or wild game such as bear or moose); incubation period 1 d-8 w; prevention and control by adequate cooking or freezing), *Trichuris trichuria* (whipworm; worldwide prevalence 350 M; especially hot, wet areas, also temperate areas), *Capillaria philippinensis, Strongyloides fuelleborni* and *Strongyloides stercoralis* (usually chronic or recurrent—40+ y; persistent in 20% of all World War II prisoners in Burma-Thailand camps and in 50% of those with symptoms), hookworm (*Ancyclostoma ceylanicum, Ancyclostoma duodenale, Necator americanus*; all tropical and subtropical countries; 700 M cases/y worldwide; transmission by skin contact with contaminated soil; incubation period 2-10 w; prevention by sanitation, wearing of shoes), *Trichostrongylus, Enterobius vermicularis* (pinworm; worldwide; commonly seen in children), *Ascaris lumbricoides* and *Ascaris suum* (150M cases/y worldwide; Africa, Asia, Latin America; 60 000 deaths/y; > 2000 cases/100,000 in China; fecal transmission; incubation period 2 mo; prevention and control by sanitation), *Anisakis simplex, Pseudoterranova, Physaloptera caucasia, Toxoplasma gondii* (225,000 estimated cases/y in USA, 50% foodborne, 21% of foodborne related deaths); larvae of flies of Order Diptera (*Calliphora vomitoria, Chrysomya chloropyga, Chrysomya putoria, Clogmia albipunctata, Eristalis tenax, Fannia canicularis, Gasterophilus haemorrhoidalis, Gasterophilus intestinalis, Gasterophilus nasalis, Musca domestica, Piophila, Sarcophaga bullata, Sarcophaga hirtipes, Sarcophaga ilerminieri, Sarcophaga peregrina, Sarcophaga ruficornis, Sarcophaga sarraceniae, Sarcophaga striata*); *human cytomegalovirus* in AIDS

Diagnosis:

***Giardia lamblia*:** vehicle drinking water, contaminated food; incubation period 1-4 w; malaise, gastric pain, malabsorption; diarrhoea > 5 d, recurrent, mucoid, fatty stools; bloating, flatulence, nausea, vomiting, anorexia, weight loss, no fever; no leucocytes or erythrocytes in stool micro; trophozoites in diarrheic and cysts in formed faeces (modified Ritchie formalin-ether concentration); trophozoites in duodenal or jejunal aspirate or biopsy; solid phase qualitative immunochromographic assay (ColorPac Giardia/Cryptosporidium; ≈ 1% false positives, no false negatives); serology for *Giardia lamblia* IgG; ELISA (sensitivity 84-98%, specificity 97-100%, positive predictive value 73%, negative predictive value 97%)

***Chilomastix mesnili*:** trophozoites in unformed and cysts in formed stools

***Cryptosporidium* and *Isospora*:** vehicle water, vegetables, fruits, unpasteurised milk; incubation period 2-28 d; usually mild and self-limited but severe clinical symptoms reported; acute onset malaise, bloating, abdominal pain and cramping, weight loss, watery mucoid diarrhoea, malabsorption ± fever, vomiting; no leucocytes or erythrocytes in stool micro; oocysts in fresh warm stools; iodine stained wet preparation; phase contrast examination of Sheather's sugar flotation concentrate; sedimentation and modified acid-fast staining; indirect fluorescent antibody; solid phase qualitative immunochromographic assay (ColorPac Giardia/Cryptosporidium; ≈ 1% false positives, no false negatives); duodenal aspirate; histology of small or large bowel biopsy

Cyclospora: incubation period 1-11 d; protracted intermittent diarrhoea (may alternate with constipation, often relapsing) in 96% (watery in 96%, mucus in 61%, no blood), flatulence in 96%, weight loss in

92%, nausea in 92%, abdominal cramps in 79%, vomiting in 53%, fever in 43%, fatigue, indigestion, malaise, bloating, anorexia, myalgia, 'flu-like' symptoms; symptoms last up to 7 w in immunocompetent and up to 4 mo in AIDS patients; Reiter syndrome and Guillain-Barré syndrome reported; characteristic unsporulated oocysts in wet film or modified acid-fast stain

Sarcocystis: usually asymptomatic; may be acute episode of abdominal pain and diarrhoea or, in prolonged infections, recurrent abdominal manifestations; patients with at least 500 flukes show rumbling on palpation of sigmoid and cecum, diarrhoea and gastric pain

***Blastocystis hominis*:** visualisation of parasite in wet films or stained by modified Ziehl-Neelsen stain

Microsporidia: incubation period 1-2 w; malabsorptive diarrhoea with bloating; no fever; systemic dissemination to liver, gall bladder, sinuses, muscle, eye and central nervous system can occur with *Encephalitozoon intestinalis*; no leucocytes or erythrocytes in stool micro; examination of stool by modified trichrome stain (technique of Weber et al) or fluorescence, Giemsa stained smear of small intestinal biopsy

Balantidium coli: may be asymptomatic, acute or chronic; alternating diarrhoea and constipation, dysentery, abdominal colic, tenesmus, nausea, vomiting; especially in malnourished children, deep penetrating ulceration of colon may be caused; fulminating dysentery, intestinal perforation, hemorrhage and shock are rare, sometimes fatal, complications; trophozoites in diarrheic and cysts in formed feces; anemia (erythrocyte count and hemoglobin may be decreased)

Schistosoma: diarrhoea in 66% of cases of acute schistosomiasis (31% bloody); urogenital disturbances; ova in faeces (acid-ether concentration) or in rectal and colonic granulomata; counterimmunoelectrophoresis, indirect hemaglutination titre; eosinophilia in all cases of acute schistosomiasis

Fasciola hepatica: vomiting, irregular fever, right upper quadrant pain, diarrhoea, jaundice, hepatomegaly; may be fatal; geographic history; dietary history; ova in feces; complement fixation test, precipitin, counterimmunoelectrophoresis, indirect haemagglutination (experimental); eosinophilia, increased ESR, erythrocyte count and hemoglobin may be decreased

Fasciolopsis buski: abdominal pain, nausea, diarrhoea with greenish-yellow stools containing undigested food; may be edema of face, abdomen and legs, dry skin and extreme prostration; may be fatal; geographic history; dietary history; ova and sometimes adult trematodes in feces; anemia (erythrocyte count and haemoglobin decreased) and eosinophilia

***Dicrocoelium hospes*:** constipation and diarrhoea, flatulence, vomiting, hepatomegaly, toxemia; presence of eggs in feces not necessarily proof of infection

***Paragonimus westermani*:** cough, hemoptysis, chest pain, epilepsy; geographic history; dietary history; ova in feces and sputum; complement fixation test; eosinophilia, anemia (erythrocyte count decreased)

***Nanophyetus salmincola*:** ingestion of salmonid fish; diarrhoea, abdominal discomfort, anorexia, vomiting, weight loss; blood eosinophilia; visualisation of ova in feces

***Opisthorchis*:** mild disease usually asymptomatic; heavy infection manifested by fever, anorexia, epigastric pain, diarrhoea, weight loss, hepatosplenomegaly, jaundice; ingestion of raw or inadequately cooked freshwater fish

***Clonorchis sinensis*:** mild infection usually asymptomatic; fever, anorexia, epigastric pain, hepatomegaly, jaundice, obstruction of bile ducts, diarrhoea, cirrhosis, portal hypertension; eating raw or inadequately cooked freshwater fish; ova in stools, bile or urine; complement fixation test, indirect hemagglutination; eosinophilia, anemia (erythrocyte count and hemoglobin may be decreased)

***Heterophyes* and *Metagonimus*:** mild disease usually asymptomatic; heavy infection characterised by diarrhoea with bloody mucoid stools, abdominal pain, neurasthenia, eosinophilia; ingestion of raw or inadequately cooked freshwater fish

***Taenia saginata*:** ingestion of beef; most frequently, disagreeable sensation in perianal area due to migratory proglottids; may be abdominal pain, hunger pains, diarrhoea, weight loss or gain, nervousness, insomnia, anorexia; incubation period 3-6 mo; at times, proglottids inside appendix or bladder causing appendicitis or cholecystitis; segments or motile proglottids may be passed; gravid segments, ova (by formalin-ether concentration), scolices in faeces; ova on cellophane swab of perianal area; serology by indirect fluorescent antibody titre; eosinophilia in 10% of cases

***Taenia solium*:** ingestion of pork; often asymptomatic, but may be manifested by vague abdominal pain, headache, indigestion, alternating diarrhoea and constipation, weight loss, insomnia, hunger pains, anorexia;

in children and debilitated adults, may be nervous manifestations (nervousness, epilepsy, mental disorders); incubation period 3-6 mo; segments may be passed; segments, ova (by formalin-ether concentration), scolices in feces or from perianal area; serology by indirect fluorescent antibody titre; eosinophilia commoner in simple enteritis than in cysticercosis

Echinococcus: cysts in liver, lung, brain, spleen, orbit, soft tissues; abdominal ultrasound or CT and CT or MRI of chest and brain

Hymenolepis: mild infection usually asymptomatic, but severe toxemia, manifested by abdominal pain, diarrhoea, headache, nasal and oral pruritus, dizziness, epileptiform convulsions and other disturbances of CNS, may occur; ova in faeces 30 d after infection; anaemia, eosinophilia

***Dipylidium caninum*:** usually asymptomatic; sometimes, epigastric pain, indigestion, loss of appetite, diarrhoea, anal pruritus

***Diphyllobothrium*:** often asymptomatic; abdominal pain and discomfort, constipation, diarrhoea, vomiting, intestinal obstruction; ingestion of uncooked freshwater fish; segments may be passed; ova or proglottids in faeces or vomitus; scolex required for species identification; if attached high in small intestine, segments vomited; occasionally produces megaloblastic anaemia with low serum B_{12}

***Trichuris trichuria*:** light infections very common and usually asymptomatic; heavy infections usually manifested by headache and abdominal pain; rectal prolapse may occur, especially in children; haemorrhagic colitis rare complication; ingestion of soil, raw vegetables or fruit; ova in faeces (modified Ritchie formalin-ether concentration); larvae and adult worms in surgical specimens of appendix and caecum; counterimmunoelectrophoresis; eosinophilia in 25% of cases, anaemia (erythrocyte count and haemoglobin may be decreased)

Capillaria philippinensis: recurrent abdominal pain and intermittent diarrhoea; severe protein-losing enteropathy with malabsorption of fats and sugars; weight loss, anorexia and vomiting common; case-fatality ratio high; several relapses over 2-3 y usual after recovery from initial attack; transmitted by eating undercooked and raw fish; microscopy of faeces for ova

***Strongyloides stercoralis*:** mild to severe gastrointestinal symptoms (mucous diarrhoea, frequently alternating with constipation; abdominal crampy pain, heartburn) in 42%, 25% asymptomatic, 22% skin complaints (recurrent pruritic rash in 25% of all World War II prisoners in Burma-Thailand), 7% pruritus ani, 4% fever; 100% mortality in untreated hyperinfection in immunocompromised; rhabditiform and occasionally filariform larvae in fresh stools (Baerman stool concentration most sensitive), duodenal aspirate; larval antigen ELISA; indirect haemagglutination; neutrophilia followed by leucopenia, up to 40% eosinophilia (83% > 400 eosinophils/μL; increased mortality with lower eosinophilia), anaemia (erythrocyte count and haemoglobin may be decreased); ELISA (sensitivity 95%)

Hookworm: usually asymptomatic; severe disease characterised by diarrhoea with blood-stained stools, epigastric pain, mental apathy or retardation, weight loss, oedema, puffy face, changes in renal function, ulcer, retarded growth; may be cardiovascular complications and secondary malabsorption syndrome; ova and larvae in faeces by brine flotation; indirect haemagglutination; iron deficiency anaemia (erythrocyte count and haemoglobin decreased), hypoproteinemia, eosinophilia

Necator americanus: initial dermatitis occurs less often; anaemia usually less severe

***Trichostrongylus*:** usually no signs or symptoms but heavy infections may result in change to mucosa, anaemia, dry skin and emaciation; ova or adult worms in stool

***Enterobius vermicularis*:** perianal pruritus, poor appetite, irritability and insomnia due to female worms migrating through anus at night, abdominal pain, dysentery, rectal prolapse; secondary migration of worms into unusual sites elicits granuloma formation in appendix, fallopian tubes and peritoneal cavity; distant metastatic spread in liver and lung and in urethra of homosexual men; ova in perianal scrapings or sticky tape preparation, occasionally in faeces; adult worms in faeces and occasionally in appendices at operation; eosinophlia common, sometimes neutrophilia

Ascaris: eosinophilia common

Anisakis*, *Pseudoterranova: ingestion of raw, pickled or undercooked fish or squid, white sushi; America, Hawaii, Netherlands, Scandinavia; fever, intestinal colic, abdominal abscess, eosinophilic granulomata; sometimes intestinal obstruction or perforation and peritonitis, occasionally throat infection; larvae in faeces and pharynx; biopsy

Trichinella spiralis: nausea, vomiting, diarrhoea and abdominal discomfort followed by fever, myalgias and periorbital oedema; serology; demonstration of larvae in muscle biopsy; increase in eosinophils

Toxoplasma gondii: serology

Intestinal Myiasis: usually transient; may be manifested by nausea, vomiting, intestinal discomfort and diarrhoea; arises through ingestion of food contaminated with larvae

***Human cytomegalovirus*:** barium study

Treatment:

***Cryptosporidium*:** none unless > 2 w; discontinuation of immunosuppressive drugs; oral rehydration in acute phase; antidiarrhoeal drugs; paromomycin 7.5 mg/kg to 500 mg orally 6 hourly, nitazoxanide (1-3 y: 100 mg, 4-11 y: 200 mg, > 11 y: 500 mg) orally 12 hourly for 3 d; immune bovine dialyzable leucocyte extract

Encephalitozoon intestinalis: albendazole 400 mg (≤ 10 kg: 200 mg) orally 12 hourly for 21 d (not in pregnant or < 6 mo)

Enterocytozoon bieneusi: fumagillin 60 mg orally daily for 14 d

***Cyclospora cayetanensis*:** cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly for 7 d in immunocompetent and 10-14 d in immunocompromised

Isospora belli: cotrimoxazole 4/20 mg/kg to 160/800 mg orally 6 hourly for 10 d, followed by 160/800 mg orally 3 times a week to prevent relapse in HIV infection

***Toxoplasma gondii*:** pyrimethamine 50-100 mg (child: 2 mg/kg to 25 mg) orally first dose then 25-50 mg daily (infants: 1 mg/kg every second or third day) for 3-6 w + sulphadiazine 1-1.5 g (child: 50 mg/kg) orally or i.v. 6 hourly for 3-4 w (clindamycin 600 mg orally or i.v. if hypersensitive) + folinic acid 3-6 mg orally daily; spiramycin 2-4 g (child: 50-100 mg/kg) orally daily for 4 w; cotrimoxazole 160/800 mg (child: 1.5/7.5 mg/kg) twice daily for 4 w

Maintenance Therapy in HIV/AIDS: pyrimethamine 25-50 mg orally daily + sulphadiazine 500 mg orally 6 hourly or 1 g orally 12 hourly (clindamycin 600 mg orally 8 hourly if hypersensitive)

Dientamoeba fragilis: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 3-7 d (not < 8 y), metronidazole 10 mg/kg to 400 mg orally 8 hourly for 3-7 d

Giardia lamblia: tinidazole 50 mg/kg to 2 g orally as single dose, metronidazole 30 mg/kg to 2 g orally daily for 3 d

Treatment Failure: metronidazole 10 mg/kg to 400 mg orally 8 hourly for 7 d

***Blastocystis hominis*:** probably none required; metronidazole 10 mg/kg to 400 mg orally 8 hourly for 7 d, metronidazole benzoate suspension 30 mg/kg/d to maximum 1.2 g/d orally in 3 divided doses for 7 d, furazolidone 150 mg orally (not for infants < 1 mo; 1 mo - 1 y: 6.25-12.5 mg; 1-4 y: 25 mg; ≥ 5 y: 50 mg) 6 hourly for several months

Balantidium coli: tetracycline 500 mg orally 6 hourly for 10 d, metronidazole 800 mg (child: 10-15 mg/kg) orally for 5 d, paromomycin 1 g (child: 11 mg/kg) every 15 minutes for 4 doses

***Schistosoma*:** praziquantel, niridazole or sodium stibogluconate + dexamethasone

***Fasciolopsis buski*:** hexylresorcinol

***Nanophyetus salmincola*:** niclosamide 2 g orally on alternate days for 3 doses, bithionol 50 mg/kg as a single dose on alternate days for 2 doses

Other Flukes: praziquantel 25 mg/kg orally 8 hourly for 1 d, tetrachloroethylene 0.1 mL/kg to 5 mL orally

Taenia: praziquantel 10 mg/kg orally as a single dose, niclosamide 2 g (child 11-34 kg: 1 g; > 34 kg: 1.5 g) in single dose chewed thoroughly then purgative 3-4 h later, paromomycin 1 g (child: 11 mg/kg) every 15 minutes for 4 doses

Hymenolepis: praziquantel 25 mg/kg orally as a single dose, niclosamide 2 g dose chewed thoroughly daily for 7 d (child: 11-34 kg: 1 g as a single dose then 500 mg daily for 6 days; > 34 kg: 1.5 g as a single dose then 500 mg daily for 6 d), paromomycin 45 mg/kg orally daily for 7 d

***Diphyllobothrium*:** niclosamide 2 g chewed thoroughly (child 11-34 kg: 1 g; > 34 kg: 1.5 g) given once as a single dose, praziquantel 10-20 mg/kg orally as a single dose, paromomycin 1 g (child: 11 mg/kg) every 15 minutes for 4 doses

Other Tapeworms: niclosamide, dichlorophen, mepacrine

***Trichuris trichuria*:** mebendazole 100 mg (≤ 10 kg: 50 mg) twice daily orally for 3 d (not in first trimester or < 6 mo), albendazole 400 mg (≤ 10 kg: 200 mg) orally daily for 3 d (not in pregnancy, lactation or < 6 mo); precede with loperamide (initial dose 4 mg, then 2 mg after each unformed stool to maximum daily dose 16 mg) if diarrhoea

***Strongyloides stercoralis*:** ivermectin 200 μg/kg orally with fatty food (not children < 5 y) on day 1 and repeat after 7-14 d (days 1, 2, 15 and 16 in immunocompromised), albendazole 400 mg (≤ 10 kg: 200 mg) orally with fatty food once daily for 3 d and repeat after 7-14 d (not in pregnancy, lactation or < 6 mo; repeat after 1 w in complicated or disseminated infections), thiabendazole 25 mg/kg to 1.5 g orally 12 hourly for 3 d (not in first trimester or < 6 mo), mebendazole

Hookworms, *Ascaris*: pyrantel embonate 20 mg/kg to 750 mg orally as a single dose (repeat after 1 w if heavy infection), mebendazole 100 mg (≤ 10 kg: 50 mg) orally twice daily for 3 d (not in first trimester or < 6 mo), albendazole 400 mg (≤ 10 kg: 200 mg) orally as single dose (not in pregnancy, lactation or < 6 mo)

Enterobius vermicularis: pyrantel embonate 10 mg/kg to 750 mg orally single dose, mebendazole 100 mg (child ≤ 10 kg: 50 mg) orally single dose (not in first trimester or < 10 kg), albendazole 400 mg (child ≤ 10 kg: 200 mg) orally single dose (not in pregnancy, lactation or < 6 mo)

***Anisakis*, *Pseudoterranova*:** thiabendazole 25 mg/kg to maximum 3 g orally twice daily for 3 d; surgery usually required

Trichinella spiralis: mebendazole

Other Helminths: thiabendazole

Prophylaxis:

Communities with Heavy Intestinal Helminth Exposure: albendazole (≤ 10 kg: 200 mg; > 10 kg: 400 mg) orally single dose every 4-6 mo to children 6 mo-12 y

***Toxoplasma gondii* in HIV/AIDS CD4 count < 200/μL:** cotrimoxazole 80/400 or 160/800 mg orally daily or 160/800 mg orally 3 times weekly

ENTEROCOLITIS

Agents: *Campylobacter* (91% *Campylobacter jejuni,* 9% *Campylobacter fetus subsp fetus*; *Campylobacter coli* in some geographical areas; also *Campylobacter concisus, Campylobacter hyointestinalis, Campylobacter lari, Campylobacter upsaliensis, Helicobacter cinaedi, Helicobacter fennelliae;* 5% of cases of diarrhoea, 8% of infectious diarrhoea, 43% of infectious diarrhoea in adults; ≈ 13,000 notified cases/y in Australia (≈ 37% in Victoria); incidence 20/100,000 in USA (estimated 2.5 M total cases, 80% foodborne, 5% of foodborne related deaths); sporadic disease from environment (up to 50%), raw and undercooked poultry, beef and gravy, salad vegetables, bottled water; outbreaks (0.9% of foodborne related outbreaks, 0.6% of cases, 3% of deaths) from unpasteurised milk (present in 40% of dairy cattle) or juice or soft cheeses and contaminated water), *Staphylococcus aureus* (usually following tetracycline treatment), *Bacteroides*; see also **BACILLARY DYSENTERY, INFANTILE DIARRHOEA, TRAVELLERS' DIARRHOEA, BACTERIAL GASTROENTERITIS, PROCTITIS, ENTERITIS, NECROTISING ENTEROCOLITIS**; may also be due to spirochaetes and several fungi (*Candida, Cryptococcus neoformans, Paracoccidioides brasiliensis, Histoplasma capsulatum, Blastomyces dermatitidis, Sporothrix schenckii, Aspergillus, Coccidioides immitis, Mucoraceae)*

Diagnosis:

Campylobacter: cases present with clinical, sigmoidoscopic, radiographic and histologic features similar to ulcerative colitis—often bloody diarrhoea (6% of bloody diarrhoea; watery diarrhoea in 63%, macroscopic mucus in 55-87%, macroscopic blood in 7-30%, microscopic blood in 35%) and severe abdominal pain and cramps; fever in 28-90%; incubation period 2-5 d; duration of illness 2-10 d; polymorphonuclears in 96% (1-10/hpf in 56%), pH acidic in 68%; Gram stain and culture (Skirrow's medium or equivalent directly and after enrichment in medium of Martin et al microaerophilically at 42°C, mannitol salt agar aerobically at 35°C, blood agar with vancomycin and kanamycin anaerobically) of faeces

Treatment:

***Campylobacter*:** erythromycin 10 mg/kg to 500 mg or erythromycin ethyl succinate 20 mg/kg to 800 mg orally 6 hourly for 5-7 d; norfloxacin 10 mg/kg to 400 mg orally 12 hourly for 5 d (13% require treatment, though treatment in all cases shortens symptomatic period, carriage and shedding; Guillain-Barré syndrome possible sequela)

***Staphylococcus aureus*:** i.v. cloxacillin + oral neomycin

***Bacteroides*:** metronidazole

NECROTISING ENTEROCOLITIS (ENTERITIS NECROTICANS, PIG-BEL): common in Papua New Guinea and China
Agent: *Clostridium perfringens C*, *Clostridium butyricum*
Diagnosis: severe abdominal pain developing up to 4 d after a protein meal, often associated with vomiting, abdominal distension and either mild diarrhoea with blood or constipation; culture of surgical specimens and typing of isolate
Treatment: surgical resection of affected length of intestine; if surgery impossible, metronidazole 500 mg (child: 7.5 mg/kg) i.v. 8 hourly or 1 g (child: 500 mg) rectally 8 hourly
NEONATAL NECROTISING ENTEROCOLITIS: 1-7.5% of neonates; significantly higher rates in infants given amoxycillin-clavulanate
Agents: *Escherichia coli*, *Klebsiella pneumoniae*
Diagnosis: clinical; X-ray (pneumotosis intestinalis); platelet count < 100,000/μL
Treatment: withdrawal of enteric feeding; oral and parenteral aminoglycoside
Prophylaxis: sodium deoxycholate
PSEUDOMEMBRANOUS COLITIS AND ANTIBIOTIC-ASSOCIATED DIARRHOEA: 10% of infective diarrhoea in adults
Agents: *Clostridium difficile* (necrotising enterocolitis, 90% of pseudomembranous colitis, 30% of antibiotic-associated diarrhoea), *Klebsiella oxytoca* (hemorrhagic colitis), *Staphylococcus aureus* (antibiotic-associated diarrhoea)
Diagnosis:

***Clostridium difficile*:** abdominal pain, fever, nausea, vomiting, diarrhoea; feces may be blood-stained; history of antibiotic treatment (especially clindamycin and third generation cephalosporins) or antineoplastic chemotherapy; microtitre cytotoxicity toxin assay of faeces (5 d old human foreskin fibroblast or WI-38 cells; read after 4 and 24 h; sensitivity 97-100%, specificity 95%); culture of feces (sensitivity 89%, specificity 74%); counterimmunoelectrophoresis of faeces (antiserum to toxin absorbed with cells; sensitivity 41-100%, specificity 78-100%); ELISA (Premier Toxin A and B most sensitive commercial kit); latex agglutination (sensitivity 88-91%, specificity 91-99%); flexible sigmoidoscopy

***Staphylococcus aureus*:** profuse watery diarrhoea with dehydration; feces culture
Treatment (*Clostridium difficile*): cessation of antibiotic treatment; metronidazole 10 mg/kg to 400 mg orally 8 hourly for 7-10 d

Metronidazole Intolerant: bacitracin 20,000-25,000 U orally 6 hourly for 7-10 d, fusidic acid

Unresponsive, Relapsing or Severe: vancomycin 3 mg/kg to 125 mg orally 6 hourly for 7-10 d ± *Saccharomyces boulardii*

Severely Ill with Toxic Megacolon: metronidazole 12.5 mg/kg to 500 mg i.v. 12 hourly + vancomycin 12.5 mg/kg to 500 mg orally or via nasogastric tube 6 hourly for 10 d; resection of the inflamed colon may be required

Prophylaxis: 100 g *Saccharomyces boulardii* or other probiotic drink twice daily during course of antibiotics and for 1 w after
HEMORRHAGIC COLITIS
Agent: shigatoxin-producing *Escherichia coli* (3% of bloody diarrhoea; incidence 3/100,000 in USA (110,000 estimated total cases, 85% foodborne, 1% of foodborne related deaths; 3% of foodborne disease outbreaks, with 4% of cases and 28% of deaths; undercooked meat (ground beef) or poultry, unpasteurised milk or juice, unpasteurised soft cheeses, unchlorinated water supplies, animal contact at petting zoo, farm animal hides; most sporadic cases from environment); mainly serotype O157:H7; cases due to O111:H8 in Australia; also O173:H55 and O166); may lead to development of hemolytic uremic syndrome or thrombotic thrombocytopenic purpura, particularly in children < 15 y and adults > 65 y (hypochlorhydria and coincidental antibiotics significant risk factors)
Diagnosis: severe, often bloody, diarrhoea, abdominal pain and vomiting following ingestion of undercooked beef, unpasteurised milk or juice, raw fruits and vegetables, salami, salad dressing, contaminated water; incubation period 1-8 d; duration of illness 5-10 d; fever in ≈ 1/3 cases, more common in < 4 y; culture of feces on sorbitol MacConkey agar or Rainbow Agar VTEC + serotyping of isolate; toxin assay (false positives)
Differential Diagnosis: inflammatory bowel disease, polyps, Meckel's diverticulum, intussusception, coagulopathy, infectious enteritis
Treatment: supportive; monitor renal function, hemoglobin and platelets closely; antibiotics may be harmful (though recent research suggests azithromycin may be beneficial)

TYPHLITIS: necrotising colitis in neutropenics, especially children with acute leukemia
Agents: *Escherichia coli, Enterobacter cancerogenus, Morganella morganii, Pseudomonas aeruginosa, Clostridium,* other Gram negative bacilli
Diagnosis: temperature ≥ 38.5ºC in all, diarrhoea in 92% (bloody in 54%), nausea in 75%, vomiting in 67%, decreased bowel sounds in 62%, rebound/guarding in 58%, abdominal distension in 54%; computed tomography and ultrasonography of pelvis show pathognomonic bowel thickening; may progress to perforation, peritonitis, fistulous communications and sepsis; potentially lethal
Treatment: surgical excision if clinical deterioration; appropriate antibiotics

CYTOMEGALOVIRAL COLITIS
Agent: *human cytomegalovirus*
Diagnosis: barium enema; IgG seroconversion; viral culture
Treatment: valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly or 180 mg/kg/d by continuous i.v. infusion for 2 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria ≤ 2+ and creatinine clearance ≥ 55 mL/min) then as above every 2 w

GASTROINTESTINAL ANTHRAX (MYCOSIS INTESTINALIS; SPLENIC FEVER IN ANIMALS): form of anthrax acquired by man through consumption of contaminated raw or undercooked meat or by dissemination from pulmonary or cutaneous forms; no cases in USA; considered rare but probably greatly underreported in rural endemic areas (Thailand, India, Iran, Gambia, Uganda); case-fatality rate 25-60%
Agent: *Bacillus anthracis*
Diagnosis: oropharyngeal anthrax: fever and toxemia, inflammatory lesions in oral cavity or oropharynx, enlargement of cervical lymph nodes, edema of soft tissue of cervical area; lower areas: abdominal distress characterised by nausea, vomiting, anorexia, fever and malaise followed by abdominal pain, hematemesis, fever and, sometimes, bloody diarrhoea; incubation period 2 d to weeks; duration of illness weeks; Gram stain and culture of stools; blood cultures; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test
Treatment: procaine penicillin 600 000 U 12 hourly i.m. (child: 25 000-30 000 U/kg daily in 2 divided doses) for 5-7 d, ciprofloxacin, tetracycline 500 mg orally 4 hourly for 5 days, erythromycin 500 mg orally 6 hourly (child: 30 mg/kg/d in 4 divided doses) for 5 d

PROCTITIS
Agents: *Neisseria gonorrhoeae* (anorectal gonococcal disease of the rectal columnar mucosa arising either by direct extension from a urogenital process (in female) or as the result of primary infection; frequently inapparent but may give rise to severe proctitis), *Simplexvirus*, *Chlamydia trachomatis* (LGV), *Treponema pallidum*, single cases due to *Neisseria cinerea* (in 8 year old boy) and *Plesiomonas shigelloides* (with fatal septicemia); also non-specific proctitis (analogous to ulcerative colitis)
Diagnosis: Gram stain and bacterial and viral culture of pus; immunofluorescence; biopsy; CT scan
Treatment:

Neisseria gonorrhoeae: ceftriaxone 125 mg i.m. + doxycycline 100 mg orally twice a day for 7 d
Treponema pallidum: penicillin + probenecid
Chlamydia trachomatis: tetracycline, doxycycline, erythromycin
Simplexvirus: famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d
Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly
Non-specific: prednisolone suppositories

PROCTOCOLITIS
Agents: *Campylobacter jejuni*, *Campylobacter hyointestinalis, Helicobacter cinaedi* and *Helicobacter fennelliae* (homosexual men), *Shigella, Entamoeba histolytica, Chlamydia trachomatis* (LGV; rare), *human cytomegalovirus* in AIDS
Diagnosis: wet mount, Gram stain and culture of pus
Treatment:

Campylobacter, Helicobacter: erythromycin

Human cytomegalovirus: valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria ≤ 2+ and creatinine clearance ≥ 55 mL/min) then as above every 2 w

Shigella: ceftriaxone 125 mg i.m. for 7 d

Chlamydia trachomatis: tetracycline, doxycycline, erythromycin

Entamoeba histolytica: metronidazole

ACUTE ABDOMEN SYNDROMES

Agents: infectious causes include (in order of frequency) acute appendicitis, diverticulitis of colon, acute tonsillitis (in young children), pneumonia, herpes zoster (T8-12), Bornholm disease, intestinal worms, acute hemolytic crisis in malaria

Diagnosis: examination of patient; X-rays of chest and abdomen; blood, urine and feces examination

Treatment: dependent on cause

ABDOMINAL CRAMPS are very severe in staphylococcal food poisoning, severe in 98% of cases of *Salmonella* gastroenteritis, 95% of *Shigella* infections and 84% of *Campylobacter* enteritis, and moderate in 67% of cases of cryptosporidiosis. Abdominal cramps also occur in 92% of *Vibrio parahaemolyticus* and 87% of enterotoxigenic *Escherichia coli* infections, in 82% of cases of traveller's diarrhoea, 79-86% of *Norwalk virus* gastroenteritis, 74% of *Clostridium perfringens* food poisoning, 63% of *Aeromonas hydrophila* infections, 59% of cholera cases, and 25% of trichinosis, as well as in other cases of acute infectious nonbacterial gastroenteritis, in food poisoning due to *Salmonella enteric subsp enteric serovar Arizona*, *Bacillus cereus*, *Enterobacteriaceae, Pseudomonas aeruginosa, Enterococcus faecalis, Enterococcus faecium* and *Yersinia enterocolitica*, in botulism, diphyllobothriasis, giardiasis, psittacosis, tick paralysis, *Vibrio cholerae* non-01 infections and chemical poisoning.

ABDOMINAL DISCOMFORT of lesser degree is also seen in 22% of hospitalised measles cases, intermittently in rabies, and in echinococcosis and wound botulism.

ABDOMINAL DISTENSION is a feature of 66% of cases of typhoid fever, 14% of peritonitis, 6% of amoebic liver abscess, and also occurs in diphyllobothriasis, giardiasis and necrotising enterocolitis.

ABDOMINAL GUARDING is prominent in 23% of cases of amoebic liver abscess and 18% of peritonitis.

ABDOMINAL MASS is found in 17% of cases of pyogenic liver abscess, in 10% of amoebic liver abscess, and in echinococcosis (non-tender).

ABDOMINAL RIGIDITY is associated with chromobacteriosis and spider bite (*Latrodectus mactans* et al)

ABDOMINAL SYMPTOMS also occur in legionellosis.

COLIC is particularly associated with ascariasis and (in severe form) shigellosis.

CROHN'S DISEASE: found more often in children than in adults

Agent: ? *Mycobacterium avium subsp paratuberculosis*

Diagnosis: fever, abdominal pain, diarrhoea, weight loss, often resembling acute appendicitis; failure to isolate causative organism; macroscopic appearance of gut (involvement of terminal ileum, often with extensions to proximal colon; crypt abscesses and microgranulomas) when abdomen opened for suspected appendicitis

APPENDICITIS

Agents: coliforms, mixed anaerobes, *Streptococcus pyogenes*, *Streptococcus viridans,* staphylococci, *Arcobacter butzleri, Campylobacter jejuni, Aggregatibacter segnis, Streptococcus milleri, Enterobius vermicularis, Entamoeba histolytica, Taenia saginata, Angiostrongylus costaricensis, Ascaris lumbricoides, Trichuris trichuria, Schistosoma mansoni, Strongyloides stercoralis, Cryptosporidium, Balantidium coli* (exceedingly rare)

Diagnosis: usually based on clinical symptoms + neutrophilia (96% of cases > 10,000 leucocytes/μL or > 75% neutrophils) and absence of other infection such as UTI; barium enema, laparoscopy, sonography; *Enterobius vermicularis*, a rare cause, produces eosinophilia as well as neutrophilia; cultures of swabs taken at surgery may be performed to confirm diagnosis and to provide the basis for therapy if peritonitis should develop

Amoebic Appendicitis: diarrhoea with blood-stained stools

Angiostrongylus costaricensis: intraabdominal mass, usually localised in right iliac fossa; in most cases, lesions localised in appendix but, at times, they may reach terminal portion of ileum, cecum and colon; abdominal pain, anorexia, vomiting and fever that may persist for 2 mo; abdomen distended; marked leucocytosis with eosinophilia of 11-81% may be present

Treatment: surgery after 1 d ceftizoxime

DIVERTICULITIS

Agents: anaerobes (*Bifidobacterium, Eubacterium*), enterics

Diagnosis: radiology; culture not necessary

Treatment: dietary restriction; fluids (oral or i.v.); surgery if necessary; if perforation, treat as for **PERITONITIS;** amoxycillin/clavulanate 875/125 mg orally 12 hourly for 5-10 d; metronidazole 400 mg orally 12 hourly + cephalexin 500 mg orally 6 hourly for 5-10 d

Immediate Penicillin Hypersensitive: metronidazole 400 mg orally 12 hourly + cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly for 5-10 d

Prophylaxis: psyllium hydrophilic mucilloid

BILIARY CIRRHOSIS

Agents: *Clonorchis sinensis*, *Fasciola gigantica, Fasciola hepatica, Opisthorchis viverrini* (Thailand and Laos), *Opisthorchis felineus* (Eastern Europe)

Diagnosis: geographic history; dietary history; ova in stools, biliary drainage, duodenal drainage; indirect hemagglutination, counterimmunoelectrophoresis, complement fixation test; anti-mitochondrial antibody test +++

Fasciola: fever, pain in epigastrium or right hypochondrium, anorexia, nausea, vomiting, sometimes alternating diarrhoea and constipation, hepatomegaly, biliary colic; occasionally halzoun; often eosinophilia; may be asymptomatic

***Clonorchis sinensis*, *Opisthorchis*:** fever, abdominal pain, jaundice

Treatment: bithionol 30-50 mg/kg orally on alternate days for 20-30 d (only treatment for *Fasciola*), praziquantel 25 mg/kg orally 8 hourly for 5-8 d, metronidazole 1.5 g orally in divided doses daily

CHOLECYSTITIS

Agents: 58% *Escherichia coli*, 34% *Enterococcus faecalis*, 23% *Enterobacter,* 19% *Clostridium perfringens* (emphysematous in older diabetic males), 14% *Klebsiella oxytoca,* 11% *Klebsiella pneumoniae,* 9% α-hemolytic streptococci; other streptococci (including *Streptococcus milleri*), staphylococci, other coliforms, anaerobes; rarely, *Pseudomonas*, *Campylobacter*, *Achromobacter xylosoxidans*, *Vibrio metschnikovii, Plesiomonas shigelloides*, *Haemophilus aprophilus*, *Desulphovibrio desulfuricans, Listeria monocytogenes, Ascaris lumbricoides*, *Clonorchis sinensis*, *Opisthorchis felineus*, *Opisthorchis viverrini*, *Cryptosporidium*, *Taenia saginata*; *human cytomegalovirus* and *Candida* in AIDS

Diagnosis: clinical; radiographic; culture of bile and other surgical specimens

Treatment: cholecystectomy +

***Pseudomonas*:** gentamicin

***Campylobacter*:** erythromycin

Other Bacteria: amoxy(ampi)cillin 25 mg/kg to 1 g i.v. 6 hourly + gentamicin 4-6 mg/kg i.v. as single daily dose (penicillin hypersensitive or gentamicin contraindicated: ceftriaxone 25 mg/kg to 1 g i.v. once daily or cefotaxime 25 mg/kg to 1 g i.v. 8 hourly) + metronidazole 400 mg orally 2 hourly if biliary obstruction till afebrile; follow with amoxycillin-clavulanate 500 mg orally 8 hourly if required till afebrile 48 h and normal neutrophil count

***Clonorchis sinensis*, *Opisthorchis*:** praziquantel 25 mg/kg orally 8 hourly for 1 d, chloroquine phosphate 600 mg base orally daily for 6 w

Other Helminths: praziquantel, thiabendazole

ASCENDING CHOLANGITIS

Agents: *Escherichia coli, Enterobacter, Klebsiella, Pseudomonas,* anaerobes

Diagnosis: right upper quadrant pain, fluctuating jaundice, swinging pyrexia, rigors, leucocytosis, raised serum albumin and alkaline phosphatase, bacteremia

Treatment: relief of biliary obstruction; amoxy/ampicillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin 4-6 mg/kg (child < 10 y: 7.5 mg/kg; ≥ 10 y: 6 mg/kg) i.v. daily for up to 3 d (adjust dose for renal function) + metronidazole 12.5 mg/kg to 500 mg i.v. if previous biliary tract surgery or known biliary obstruction, then (when afebrile) amoxycillin + clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 12 hourly for total of 7 d

Penicillin Hypersensitive or Gentamicin Contraindicated: ceftriaxone 25 mg/kg to 1 g i.v. daily, cefotaxime 25 mg/kg to 1 g i.v. 8 hourly

Lack of Response to 3 d i.v. Therapy: piperacillin + tazobactam 100 + 12.5 mg/kg to 4 + 0.5 g i.v. 8 hourly, ticarcillin + clavulanate 50 + 1.7 mg/kg to 3 + 0.1 g i.v. 6 hourly

PANCREATITIS

Agents: *mumps virus*, coxsackievirus B (may result in diabetes), coliforms (usually complicating chronic non-infectious cases), *human cytomegalovirus* (59% of cases in AIDS), adenovirus, *Cryptococcus neoformans* (18% of cases in AIDS), *Mycobacterium avium-intracellulare* (14% of cases in AIDS), *Toxoplasma gondii* (7% of cases in AIDS), *Mycobacterium tuberculosis* (uncommon), *Ascaris lumbricoides*; also gallstones, alcohol, medicines (2-5%)
Diagnosis: serology; viral culture of saliva; histology and culture of biopsy; check for abscess formation; serum aldolase inconsistently increased, serum amylase increased, serum leucine aminopeptidase inconsistently increased, serum lipase increased; endoscopic retrograde cholangiopancreatography
Treatment:

***Human cytomegalovirus*:** valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria $\leq$ 2+ and creatinine clearance $\geq$ 55 mL/min) then as above every 2 w

Other Viral: non-specific

Coliforms: amoxycillin-clavulanate

***Cryptococcus neoformans*:**

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w $\pm$ flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

***Mycobacterium avium-intracellulare*:** ethambutol 15 mg/kg orally daily (not < 6 y) + clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly or azithromycin 10 mg/kg to 500 mg orally daily + rifampicin 10 mg/kg to 600 mg orally daily or rifabutin 5 mg/kg to 300 mg orally daily

***Toxoplasma gondii*:** pyrimethamine 50-100 mg (child: 2 mg/kg to 25 mg) orally first dose then 25-50 mg daily (infants: 1 mg/kg every second or third day) for 3-6 w + sulphadiazine 1-1.5 g (child: 50 mg/kg) orally or i.v. 6 hourly for 3-4 w (clindamycin 600 mg orally or i.v. if hypersensitive) + folinic acid 3-6 mg orally daily; spiramycin 2-4 g (child: 50-100 mg/kg) orally daily for 4 w; cotrimoxazole 160/800 mg (child: 1.5/7.5 mg/kg) twice daily for 4 w

Maintenance Therapy in HIV/AIDS: pyrimethamine 25-50 mg orally daily + suphadiazine 500 mg orally 6 hourly or 1 g orally 12 hourly (clindamycin 600 mg orally 8 hourly if hypersensitive)

Severe Necrotising: meropenem 500 mg i.v. 8 hourly for 7 d, imipenem 500 mg i.v. 6 hourly for 7 d, piperacillin + tazobactam 4 + 0.5 g i.v. 8 hourly for 7 d

Ascaris lumbricoides: mebendazole, albendazole

Prophylaxis:

***Mycobacterium avium* Complex in HIV/AIDS (CD4 cell count < 50/µL):** azithromycin 1.2 g orally weekly, clarithromycin 500 mg orally 12 hourly, rifabutin 300 mg orally daily

***Toxoplasma gondii* in HIV/AIDS (CD4 Count < 200/µL):** cotrimoxazole 80/400 or 160/800 mg orally daily or 160/800 mg orally 3 times weekly

Pancreatic Abscess: 3-4% of acute pancreatitis cases; mortality $\approx$ 100% untreated, $\approx$ 40% treated
Agents: *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Salmonella typhi,* coliforms, *Haemophilus influenzae*, *Eikenella corrodens*, *Ochrobactrum anthropi*, *Plesiomonas shigelloides* (1 case postoperative), *Candida albicans* (very rare)
Diagnosis: ultrasound; Gram stain, Grocott-Gomori methenamine-silver stain and culture of aspirate
Treatment:

Bacteria: surgery + amoxycillin-clavulanate

***Candida albicans*:** drainage + amphotericin B

Chapter 3

Infections of the Urinary Tract

URINARY TRACT INFECTION

Urinary tract infection constitutes 0.9% of ambulatory care visits in the USA (≈ 6M/y) and is the most common bacterial infection.

The prevalence of UTI varies with age and sex. In the < 1 y group, prevalence in both sexes is ≈ 1% and is related to congenital urologic abnormalities. At 1 - 5 y, the prevalence increases in females but remains < 5%, while that in males is < 1%. In both sexes, infections are related to congenital urologic abnormalities, vesiculoureteral reflux and (in males) an intact foreskin. Prevalence rates remain the same in the 6 - 15 y age group, with nearly all infections related to vesiculoureteral reflux.

In the 16-35 y age group, prevalence in females increases to ≈ 20%; these infections are usually associated with sexual intercourse and involve organisms colonising the colon and perineum (other factors associated with increased frequency are first degree female relative with UTI, nonsecretor status, prior UTI, spermicide use and diaphragm use). In this age group, 14% of women with symptoms of urinary tract infection have a sexually transmitted disease, while only half are urine culture positive. Therefore, screening for sexually transmitted disease should also be performed. In men, prevalence remains at < 1% and is related to complicating factors. For both sexes, risk factors for complicated UTI include current or recent hospitalisation or residence in a long-term care facility, medullary sponge kidney, nephrocalcinosis, diabetes mellitus, exposure to nosocomial pathogens, functional (neurogenic bladder, vesicourethral reflux, foreign bodies) or anatomic abnormalities of the urinary tract (bladder outlet obstruction due to calculi, congenital anomaly, benign prostatic hypertrophy, stricture, tumour; nonobstructing calculi, bladder diverticula; obstruction in the upper urinary tract due to calculi, pelvicaliceal junction obstruction, renal cyst, ureteric stricture, tumour; presence of foreign body such as ureteral stent, urethral or urinary catheter, nephrostomy tube; surgically created ileal conduit), immunosuppression, pregnancy, recent antibiotic use, recent urinary tract instrumentation, renal transplantation, renal failure, symptoms for > 7 d, use of immunosuppressive drugs.

At 36 - 65 y, prevalence increases to 35% for females and 20% for males, the increase being due mainly to gynecologic surgery and bladder prolapse in both sexes, menopause in females, and prostatic hypertrophy in males.

Prevalence in the ≥ 65 y group is 40% for females and 35% for males. These infections are almost invariably complicated and relate to gynecologic surgery, bladder prolapse, prostatic hypertrophy, incontinence, catheterisation, debility, estrogen lack.

The dangers of evaluation and treatment are related mainly to age and renal status, low in the young and high in the elderly. Prognosis in boys is relatively bad without therapy because of the high incidence of abnormalities, especially obstructive uropathy. Prognosis in girls without therapy is related mainly to reflux, infection in the presence of reflux often damaging kidneys, causing clubbing and scarring, and therapy protecting the kidneys. Long-term antimicrobial prophylaxis is probably justified in young girls with nonrefluxing ureters who have had 3 or 4 recurrences of urinary tract infection. Surgical correction of ureterovesical reflux in girls with recurrent urinary tract infections is recommended only if good control of the infection cannot be obtained with antimicrobial therapy. In young and middle-aged males, prognosis without therapy is relatively bad because of the presence of anomalies. At least 25% of women with bacteriuria in early pregnancy develop acute pyelonephritis later in pregnancy and this group should be screened and bacteriuria eliminated. In other adult females, prognosis without therapy is good. Women with recurrent infections, repeated infections with the same organism which resists eradication, clinical evidence of pyelonephritis, infection by unusual organisms, poor response to treatment, or infections associated with persistent hematuria should be evaluated radiographically. In children and men, it is mandatory to look for surgically correctable abnormalities such as obstructive uropathy and stones.

Causes of unresolved bacteriuria include bacterial resistance to the drug selected for treatment, development of resistance by initially susceptible bacteria, bacteriuria caused by two different bacterial species with mutually exclusive susceptibilities, rapid reinfection with a new resistant species during therapy for the

original susceptible organism, azotemia, papillary necrosis from analgesic abuse, giant staghorn calculi in which the 'critical mass' of susceptible bacteria is too great for antimicrobial inhibition.

Causes of bacterial persistence include infected renal calculi, chronic bacterial prostatitis, unilateral infected atrophic pyelonephritis, infected pericalyceal diverticula, infected nonrefluxing ureteral stumps following nephrectomy for pyelonephritis, medullary sponge kidneys, infected urachal cysts, infected necrotic papillae from papillary necrosis.

ACUTE CYSTITIS: infection of the bladder accompanied by clinical symptoms; 1% of new episodes of illness in UK; 10 - > 50% of cases represent occult pyelonephritis; may be emphysematous in diabetics

Agents: *Escherichia coli* (89% of infections in pregnant women, 72% of all cases, 66% of recurrent infections, 58% of outpatient female, 48% of hospitalised female, 42% of outpatient male, 29% of hospitalised male patients), *Staphylococcus saprophyticus* (21% of outpatient female, 0.9% of hospitalised female, 0.7% of outpatient male, 0.4% of hospitalised male patients), *Klebsiella/Enterobacter* (14% outpatient male, 12% hospitalised male and female, 8% outpatient female cases), *Proteus* (13% hospitalised male, 10% hospitalised female and outpatient male, 10% of recurrent infections, 3% of outpatient female cases), enterococci (12% hospitalised male, 9% outpatient male, 7% hospitalised female, 2% outpatient female cases), *Staphylococcus epidermidis* (6% outpatient male, 5% hospitalised male, 3% hospitalised female, 2% outpatient female cases), *Pseudomonas* (5% outpatient male, 4% hospitalised male, 0.9% hospitalised female, 0.1% outpatient female cases), *Staphylococcus aureus* (4% hospitalised male, 3% outpatient male, 0.7% hospitalised female, 0.6% outpatient female cases), *Streptococcus agalactiae* (2% hospitalised male and female, 0.8% outpatient female, 0.7% outpatient male cases; urinary tract abnormalities in 60%, chronic renal failure in 26%), yeasts (mainly *Candida albicans*; 0.9% hospitalised male, 0.7% hospitalised female, 0.3% outpatient female cases); *Corynebacterium urealyticum* (immunosuppressed, urologic procedures, previous antimicrobials, age > 66 y), *Actinobacillus actinomycetemcomitans* (in association with endocarditis), *Ureaplasma urealyticum*, *Gardnerella vaginalis*, *Mycoplasma hominis, Streptococcus mitis, Bacteroides fragilis, Agrobacterium tumefaciens* (non-functioning kidney), *Alcaligenes faecalis* (nosocomial), *Achromobacter xylosoxidans*, *Citrobacter*, *Enterobactre agglomerans, Serratia marcescens, Aeromonas* (occasional), *Haemophilus influenzae* (non-type b and nontypeable), *Schistosoma bovis, Mycobacterium avium-intracellulare* (rare cases in renal transplant recipients)

Diagnosis: frequency in 89% of cases, urgency in 82%, dysuria in 25%, suprapubic tenderness; dysuria and frequency without vaginal irritation gives probability of 90%; dipstick (nitrite sensitivity 25%, specificity 90%; leucocyte esterase); bacteria on Gram stain sensitivity 80%, specificity 90%; micro (leucocytes $\pm$ bacteria $\pm$ erythrocytes) and culture (30-40% > 10^5 cfu/mL) of midstream urine; culture of bladder aspiration urine for low counts and fastidious species in culture negative symptomatic patients; those with risk factors above (under **URINARY TRACT INFECTION)** should have serum creatinine concentration for baseline assessment of renal function and ultrasound examination of the urinary tract if structural anomaly or obstruction is suspected

Treatment: trimethoprim 300 mg orally daily for 3 d (non-pregnant women) or 14 d (men) or 4 mg/kg to 150 mg orally 12 hourly for 5 days (children), cephalexin 500 mg orally 12 hourly for 5 d (non-pregnant women) or 10 d (pregnant women) or 14 d (men) or 12.5 mg/kg to 500 mg orally 12 hourly for 5 d (children), amoxycillin-clavulanate 500/125 mg orally 12 hourly for 5 d (non-pregnant women) or 10 d (pregnant women) or 14 d (men) or 12.5/3.1 mg/kg to 500/125 mg orally 12 hourly for 5 d (children), nitrofurantoin 50 mg orally 6 hourly for 5 d (non-pregnant women) or 10 d (pregnant women) or 14 d (men), cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly for 5 d (children); if resistant to all above agents, norfloxacin 400 mg orally 12 hourly for 3 d (non-pregnant women) or 14 d (men), levofloxacin 250 mg daily for 3 d (non-pregnant women)

Remote Areas:

Children ≤ 10 y: gentamicin 5 mg/kg i.m. single dose, cefaclor syrup orally 8 hourly for 7-10 d, cotrimoxazole orally 12 hourly for 7-10 d, trimethoprim orally daily for 7-10 d

Females > 10 y: nitrofurantoin 200 mg orally as single dose, trimethoprim 600 mg orally as single dose or 300 mg orally daily for 3 d

Males > 10 y: cephalexin 500 mg orally 8-12 hourly for 7-14 days, amoxycillin-clavulanate 250/125 mg orally 8 hourly for 7-14 d, trimethoprim 300 mg orally daily for 7-14 d

Recurrent Infection: trimethoprim 6 mg/kg to 300 mg orally once daily for 10-14 d, amoxycillin-clavulanate 10/2.5 mg/kg to 250/125 mg orally 8 hourly for 10-14 d; if resistance to both above agents, norfloxacin 400 mg orally 12 hourly (not in children or pregnant) or hexamine hippurate 1 g orally twice daily for 10-14 d (+ ascorbic acid 1 g orally twice daily if urine alkaline); recent promising trials of multivalent pessary vaccine

Klebsiella: cefotaxime 1 g i.v. 12 hourly (child: 25 mg/kg i.v. 8 hourly), norfloxacin 400 mg orally 12 hourly (not pregnant or child)

***Pseudomonas aeruginosa*:** norfloxacin 400 mg orally 12 hourly (not pregnant or child), tobramycin 1.3 mg/kg (child: 1.5-2.5 mg/kg) 8 hourly, ceftazidime 500 mg (child: 50 mg/kg) i.v. daily in divided doses

Burkholderia cepacia: imipenem

***Corynebacterium urealyticum*:** vancomycin

***Candida* (High Risk Patient with Localised Infection):** fluconazole 5 mg/kg to 200 mg orally daily for 7 d

Prophylaxis:

Recurrent Infections in Females Related to Sexual Intercourse: nitrofurantoin 50 mg orally or cephalexin 250 mg orally or trimethoprim 150 mg orally within 2 h after intercourse; cranberry juice

Recurrent Cystitis Not Related to Sexual Intercourse: nitrofurantoin 1 mg/kg to 50 mg orally nightly for 3-6 mo, cephalexin 12.5 mg/kg to 250 mg orally nightly for 3-6 mo, trimethoprim 4 mg/kg to 150 mg orally nightly for 3-6 mo, cotrimoxazole 4 + 20 mg/kg to 160 + 800 mg orally nightly (children if suitable trimethoprim formulation not available); intravaginal estrogen in postmenopausal women

Cirrhotic Patient with Gastrointestinal Bleeding: norfloxacin 400 mg orally commencing 1 h before endsocopy and then 12 hourly for 1-2 d or if oral therapy not feasible ciprofloxacin 400 mg i.v. at time of induction and then 12 hourly for 1-2 d

Acute Pyelonephritis: inflammatory process of the renal parenchyma; 0.07% of new episodes of illness in UK

Agents: *Escherichia coli* (may, rarely, cause acute renal failure, especially when NSAIDs administered), *Proteus*, *Staphylococcus aureus, Staphylococcus saprophyticus,* other coagulase negative staphylococci, *Enterococcus faecalis, Pseudomonas aeruginosa, Stenotrophomonas maltophilia* (associated with hospitalisation and antimicrobial therapy), *Salmonella* (in renal transplant recipients), *Campylobacter*, *Streptococcus agalactiae*, *Mycoplasma hominis* (rare), others

Diagnosis: dysuria, fever and chills, loin pain, costovertebral tenderness, nausea and vomiting, bacteremia, suprapubic tenderness ± urgency, frequency; leucocytosis present or absent; increased ESR; C-reactive protein present; blood procalcitonin elevated; micro (bacteria ± leucocytes ± erythrocytes ± leucocyte casts) and culture of urine; note that renal bacteriuria may be intermittent and low colony counts may be significant; counterimmunoelectrophoresis of serum; radioimmunoassay (sensitivity 96%, specificity 100%); blood cultures (positive in 41% of cases of ascending pyelonephritis); those with risk factors above (under **Urinary Tract Infection)** should have serum creatinine concentration for baseline assessment of renal function and ultrasound examination of the urinary tract if structural anomaly or obstruction is suspected

Treatment: ultrasonogram and cystogram in child with first episode

***Stenotrophomonas maltophilia, Campylobacter*:** cotrimoxazole

Others:

Severe: gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) + amoxy(ampi)cillin 50 mg/kg to 2 g i.v. 6 hourly for 10-14 d (cephalothin 25-50 mg/kg to 2 g i.v. 4-6 hourly if mild penicillin hypersensitivity; gentamicin alone if severe penicillin hypersensitivity)

Elderly, Renal Failure, Previous Adverse Reaction to Aminoglycoside: ceftriaxone 25 mg/kg to 1 g i.v. daily, cefotaxime 25 mg/kg to 1 g i.v. 8 hourly for 10-14 d

Mild to Moderate (Not *Pseudomonas aeruginosa*): cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 10 d (safe in pregnancy), amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for 10 d (probably safe in pregnancy), trimethoprim 4 mg/kg to 150 mg orally 12 hourly for 10 d (safety in pregnancy not established), cotrimoxazole 4 + 20 mg/kg to 160 + 800 mg orally 12 hourly for 10 d (children where suitable trimethoprim formulation not available)

***Pseudomonas aeruginosa* and Other Organisms Resistant to All Above Agents:** norfloxacin 10 mg/kg to 400 mg orally 12 hourly for 10 d or ciprofloxacin 10 mg/kg to 500 mg 12 hourly for 10 d (both drugs safety not established in pregnancy; not in children unless microbiologically necessary)

Penicillin Allergic Patient with Gram Positive Cause: vancomycin

colchicine or single dose cyclophosphamide may protect against chronic pyelonephritis in acute obstructive pyelonephritis

Prophylaxis (Cirrhotic Patient with Gastrointestinal Bleeding): norfloxacin 400 mg orally commencing 1 h before endsocopy and then 12 hourly for 1-2 d or if oral therapy not feasible ciprofloxacin 400 mg i.v. at time of induction and then 12 hourly for 1-2 d

DYSURIA-FREQUENCY SYNDROME (ACUTE URETHRAL SYNDROME)

Agents: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, Gram negative bacilli including *Haemophilus influenzae*; may result from acute cystitis, urethritis or vaginitis

Diagnosis: dysuria, frequency, urgency, $\geq$ 8 leucocytes/μL in first void urine specimen; growth of $\geq 10^2$ of an aerobic Gram negative bacillus from a midstream urine culture; culture and immunofluorescence of urethral swab; note that patients with pyuria, renal symptoms, proteinuria and microscopic hematuria but sterile cultures or colony counts of 10^4/μL may also have occult renal infection, perhaps with intermittent renal bacteriuria (culture of suprapubic aspirate may be necessary to eliminate this possibility)

Treatment:

***Neisseria gonorrhoeae*:** see **GONORRHOEA** in Chapter 4

***Chlamydia trachomatis*:** tetracycline, doxycycline, erythromycin (pregnancy: erythromycin)

Gram Negative Bacilli (Including *Haemophilus influenzae*): cotrimoxazole

Management of Women with Recurrent Nonvenereal Attacks of Dysuria-Frequency Syndrome:

Precipitated by Sexual Intercourse: scrupulous hygiene; lubricants; bladder emptying after intercourse; alternative positions; pillow under buttocks; nitrofurantoin 50 mg after intercourse; psychosexual history

Precipitated by Psychological Stress: counselling; psychosexual history; consider short course of a sedative or (if indicated) antidepressive therapy

Precipitated by Cold Weather: warm underclothing; trousers rather than skirts or dresses

Precipitated by Allergies: psychosexual history; avoid known allergens; consider antihistamines or desensitisation

Related to Menopause: psychosexual history; dienestrol pessaries (1 nightly for 1 week every 3 mo); dienestrol cream; pentovis (2 capsules twice daily for 2 w)

Related to Menstruation: scrupulous hygiene; a simple diuretic for a few days before a period starts; trial of oral contraceptives

DYSURIA WITHOUT FREQUENCY

Agents: herpes genitalis, urethritis (in 82% of gonococcal, 73% of non-gonococcal, 67% of *Haemophilus influenzae*, 75% of *Haemophilus parainfluenzae),* vaginitis (in 18% of trichomonal, 12% of other)

Diagnosis and Treatment: see Chapter 4

FREQUENCY WITHOUT DYSURIA occurs in prostatic abscess and vulvovaginal candidiasis

ASYMPTOMATIC BACTERIURIA: presence of bacteria in the urine in the absence of clinical symptoms; prevalence varies from 0.001% in infants to 25-50% in female nursing home residents; 20-60% of women with bacteriuria in early pregnancy develop acute pyelonephritis later in pregnancy and routine screening in populations in which the prevalence of asymptomatic bacteriuria is $\geq$ 5% is recommended; patients undergoing urological procedures producing mucosal bleeding should be screened beforehand and treated if positive

Agents: 60-89% *Escherichia coli*, 8% *Klebsiellla*, 0.7% *Proteus*; *Streptococcus agalactiae*, *Enterococcus, Salmonella* (in renal transplant recipients), *Citrobacter*, mixed infections

Diagnosis: cloudy urine; micro (leucocytes, bacteria, leucocyte casts present or absent) and culture of urine (pure culture $\geq 10^8$/L consistent with bacteriuria); note that, particularly in the absence of leucocytes, this condition may represent contamination, even if a pure growth of a single organism is obtained; in cases of doubt, particularly where multiple organisms, single organisms with a high probability of extraneous source (eg., *Proteus vulgaris, Citrobacter)*, or a succession of different organisms in repeat specimens, are isolated, a suprapubic aspiration may be necessary

Treatment: depends on patient's age and available safe agents; avoid repeated or prolonged courses of therapy in asymptomatic elderly females; neonates and preschool children should be treated and investigated for vesicoureteric reflux and other anatomical abnormalities; pregnant women should be treated because of risk of developing pyelonephritis; men < 60 y should be treated and investigated for chronic prostatitis; young children with vesicoureteric reflux and patients with genitourinary abnormalities that may become secondarily infected, nonfunctioning renal segments, medullary sponge kidneys, polycystic kidneys, calculi, ureteral obstruction, prostatic

hyperplasia, increased intrarenal voiding pressure, renal papillary necrosis, valvular heart disease, prosthesis or diabetes or who are immunocompromised, or those growing fungi, mycobacteria, *Klebsiella*, *Proteus mirabilis* or *Staphylococcus aureus* or undergoing genitourinary instrumentation or manipulation should be treated and investigated; others (including diabetics) do not require treatment

Chronic Bacteriuria: more or less continued presence of bacteria in the urine, due to inability to eradicate infection or to recurrent infections; possible causes include chronic pyelonephritis, chronic bacterial prostatitis (creatine and creatinine are usually increased), infected renal or bladder stones, bladder diverticulum, renal abscess, indwelling catheter

Agents: *Proteus* and *Staphylococcus saprophyticus* in infected stones; *Proteus*, *Providencia stuartii, Morganella morganii* and numerous others in indwelling catheter; mixed infections

Diagnosis: urine micro and culture (in patients with indwelling catheter, only if signs of systemic infection); prostatic localisation test for suspected chronic bacterial prostatitis

Treatment: correction of underlying cause if possible; antimicrobial treatment as indicated by susceptibility of isolates (note that clearing of infection from a patient with an indwelling catheter is virtually impossible; antimicrobial treatment should be restricted to acute episodes; a single 2 mg/kg dose of gentamicin given 30-60 minutes before changing catheter may help control infections; amdinocillin may be used in short term; most important factor is preventing blockage by encouraging adequate fluid intake and changing catheter regularly or immediately if poorly functioning or obstructed; suprapubic cather should be considered for long-term use)

Prophylaxis: nitrofurantoin 2.5 mg/kg to maximum 100 mg orally nightly (safe in pregnancy), trimethoprim 2 mg/kg to maximum 150 mg orally nightly (not in pregnancy)

Hemolytic Uremic Syndrome: most common cause of acute renal failure in children (mainly < 10 y); mortality $\approx 5\%$, sequelae in $\approx 50\%$; 24 cases in Australia in 1999

Agents: *Escherichia coli* (usually O157:H7; also O111); also *Streptococcus pneumoniae, Salmonella typhi, Shigella, Proteus,* variety of other bacteria, viruses and drugs

Diagnosis: microangiopathic hemolytic anemia (hematocrit $< 30\%$), thrombocytopenia (platelet count $\leq 160{,}000/\mu L$) and acute renal failure (blood urea nitrogen ≥ 20 mg/dL) after respiratory or gastrointestinal symptoms or bacteremia; elevated serum aminotransferases, triglycerides, bilirubin and uric acid, reduced serum protein, albumin, C3 and C4; feces culture on 0.5% sorbitol MacConkey agar (within 6 d of onset of diarrhoea) + serotyping; enzyme immunoassay; blood cultures

Treatment: red blood cells or platelet transfusions as required, dialysis if required, plasma exchange; avoid antimicrobials and antimotility agents

Genitourinary Tuberculosis: 0.6% of tuberculosis cases

Agent: *Mycobacterium tuberculosis*

Diagnosis: Ziehl-Neelsen stain and culture of urine on Lowenstein-Jensen or similar medium; red cells and neutrophilia present in urine in urinary tuberculosis; proteinuria without elevated cells occurs in non-urinary tuberculosis; tuberculin test; interferon gamma assay; ELISPOT

Treatment: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo); relief of ureteric obstruction if required

Urinary Fungal Infections: pelvic infection (including acute uteropelvic obstruction) occurs particularly in diabetics, while parenchymal disease is more common in leukemia and chronic granulomatous disease; mortality rate 57% in pediatric patients

Agents: *Candida*, *Torulopsis glabrata, Aspergillus*, *Penicillium citreum, Cryptococcus neoformans,* phycomycetes

Diagnosis: micro and culture of urine; sonography; in *Candida* infections, urethral, vulval, vaginal swabs may be necessary to exclude genital infection

Treatment: in diabetics, primary effort should be towards stabilising diabetes, though bladder irrigation with amphotericin B 5-10 mg/L or single dose of amphotericin B may be used if necessary (also with indwelling catheter); if renal insufficiency is present, radiography should be performed, any obstruction found relieved and cultures repeated; if infection persists or any evidence of pyelonephritis and/or papillary necrosis is found,

infection should be treated with flucytosine or amphotericin B; immunocompromised and paediatric patients, even if asymptomatic, should be treated with flucytosine or fluconazole 5 mg/kg to 200 mg orally daily for 7 d or amphotericin B

Urinary Viral Infections

Agents: *human rubella virus* and *human cytomegalovirus* (prenatal), *measles virus, mumps virus*, *Simplexvirus*, virus agent of other generalised viral infections, ? *Lymphocryptovirus* in infectious mononucleosis, *human adenovirus 11* (acute hemorrhagic cystitis in immunosuppressed patients), polyomaviruses in renal transplant recipients

Diagnosis: viral culture of urine; serology

Treatment: non-specific

Urinary Schistosomiasis

Agent: *Schistosoma haematobium*

Diagnosis: hematuria, dysuria, pyuria, chyluria; ova in urine, scrapings of lesions in bladder wall; severe iron deficiency anemia, eosinophilia, raised ESR; serology

Treatment: praziquantel 20 mg/kg orally for 2 doses after food 4 h apart

Post-Streptococcal Glomerulonephritis: immune mediated glomerulonephritis usually occurring 5-10 d after an upper respiratory infection or longer after the onset of a skin infection

Agents: almost invariably *Streptococcus pyogenes* (respiratory infections caused by a single type; skin infections caused by several types), occasionally Group C and Group G streptococci

Diagnosis: hematuria + edema, with hypertension and azotemia in more severe cases; anti-streptolysin O test (normal in $\approx$ 50% of cases (especially following skin infection); peaks at 2-4 w; false positives due to activity of other substances neutralising hemolytic properties of streptolysin O (eg., serum β-lipoprotein in liver disease) and bacterial growth in serum specimens); anti-deoxyribonuclease B (consistently elevated; rises later than ASOT, peaks at 4-6 w and remains elevated longer than ASOT; magnitude of response may be suppressed by antimicrobial therapy; detergents, heavy metals, azide and other chemicals interfere with enzyme and colour reaction); C'4 decreased (distinguishes from hypocomplementemic)

Treatment: supportive

Quartan Malarial Nephropathy (Malarial Nephrosis, Malaria Nephrosis, Nephrotic Syndrome of Quartan Malaria, Quartan Nephrosis): relatively rare complication of *malariae* malaria, especially in children

Agent: *Plasmodium (Plasmodium) malariae*

Diagnosis: glomerulonephritis with generalised edema, severe proteinuria and hypoproteinemia

Treatment: usually fatal

Genitourinary Myiasis: infestation of bladder, urethra and/or vagina by larvae of certain flies; rare

Agents: *Calliphora vomitoria, Chrysomya bezziana, Chrysomya chloropyga, Chrysomya putoria, Piophila, Wohlfahrtia*

Diagnosis: abdominal pain, dysuria, frequent urination, haematuria; may be urethral obstruction

Treatment: removal of larvae

Chapter 4

Infections of the Genital System

Genital Tract Infections

In the male, except for some cases of prostatitis and orchitis and the occasional infection of external genitalia by normal skin-infecting organisms, almost all infections of the genital tract are classical sexually transmitted diseases. In the female, though sexually transmitted diseases occur with more or less equal frequency, the majority of genital tract infections are not in this category, though many may be related to sexual activity. The presence of a vaginal discharge is a relatively common event and, in the majority of cases, is not primarily of infectious origin. However, overgrowth of endogenous organisms such as *Candida albicans* can set up a true vaginitis or, in the case of organisms such as *Gardnerella vaginalis*, anaerobes and coliforms, a vaginosis in which organisms colonise epithelial cells or mucus in large numbers, converting an inoffensive discharge into an offensive one. The presence of intrauterine contraceptive devices is associated with overgrowth of endogenous organisms and sometimes with true uterine infection; in the latter case, removal of the device is the essential, and usually the only necessary, treatment. Infections post-partum, post-abortion or post-surgery may resemble post-traumatic and post-surgery infections in other sites. Gynecologic infection constitutes 8% of non-bacteremic infection in older children and adults.

Gonorrhoea (Gonorrhea, Blennorrhagia): Worldwide venereal disease and important cause of neonatal infection; acute or chronic disease of urogenital tract (vulvovaginitis, endocervicitis, urethritis); extension of the disease within the urogenital tract may lead to endometritis, salpingitis, oophoritis, epididymitis, orchitis, spermatocystitis, cystitis; disease may extend to adjacent tissues, giving rise to prostatitis, bartholinitis, pelvic inflammatory disease, or become systemic; disseminated infection results from bacteremia and often causes petechial or pustular acral skin lesions, asymmetrical arthralgia, tenosynovitis or septic arthritis, occasionally perihepatitis and, rarely, endocarditis or meningitis; subclinical infections (urethral, cervical, anal, pharyngeal) are frequent; eye infections also occur; ≈ 6000 notified cases/y in Australia (steady increase); incidence 443/100,000 (1.6-2 M cases/y) in USA (13% of cases in homosexual men); 38% of male sexually transmitted disease, 31% of female; 40% incidence in homosexuals; transmission by mucous membrane contact; incubation period 1-14 d (most symptoms develop within 2-5 d); 0.04% of new episodes of illness in UK; 50-90% of female sexual partners of infected men infected after 1 exposure; once urethritis disappeared, most men not infectious; 20% of men infected after 1 exposure, 60-80% after 4 exposures; 2-50% of infants exposed during birth develop eye infections

Agent: *Neisseria gonorrhoeae*

Diagnosis: women may have no symptoms or vaginal discharge, pain on urination, spotting after sexual intercourse, lower abdominal pain; men: urethral discharge of pus, pain on urination; Gram stain (presence of Gram negative cocci inside polymorphs; sensitivity 90-95%, specificity > 95%) and culture of urethral, cervical, rectal, throat swabs (note that vaginal lubricants are inhibitory and should not be used on speculums, etc); isolates may be identified by biochemistry or DNA hybridisation; PCR or ligase chain reaction if culture not possible (sensitivity > 96%, specificity probably ≈ 100%); note possibility of salpingitis (in 10-20% of cases), endometritis, cervicitis, urethritis, Bartholinitis, epididymitis (in up to 20% of infected men without antibiotics); arthritis (85% of disseminated cases), meningitis (5% of disseminated cases), endocarditis (5% of disseminated cases), bacteremia without arthritis (5% of disseminated cases), pericarditis (2% of disseminated cases), abscesses, septic gonococcal dermatitis in complicated cases

Treatment: (since 20-60% coinfected with *Chamydia trachomatis*, CDC recommends concurrent treatment for this organism); ceftriaxone 25-50 mg/kg to 250 mg i.m. single dose + (if chlamydial infection not ruled out) azithromycin 1 g orally single dose (> 45 kg) or doxycycline 100 mg orally twice daily for 10 d (≥ 8 y) or erythromycin 50 mg/kg/d divided into 4 doses for 10-14 d (< 8 y); if prevalence of penicillin resistance is low (e.g., Northern Territory, Western Australia), amoxycillin 3 g orally as single dose + probenecid 1 g orally as single dose + azithromycin 1 g orally as single dose

Disseminated Infection:

Neonates: ceftriaxone 25-50 mg/kg/d i.v. or i.m. as single daily dose for 7 d or 10-14 d if meningitis documented, cefotaxime 25 mg/kg/d i.v. or i.m. every 12 h for 7 d or 10-14 d if meningitis documented

Others: ceftriaxone 1 g i.v every 24 h or cefotaxime 1 g i.v every 8 h or ceftozoxime 1 g i.v. every 8 h

Prevention and Control: exposure prevention; identification and treatment of cases (symptomatic and asymptomatic) and contacts

NON-GONOCOCCAL URETHRITIS (NON-SPECIFIC URETHRITIS): 39% of sexually transmitted disease in male; 3 M cases/y in USA; ≈ 14,000 notified cases/y in Australia (≈ 32% in Queensland); 25% incidence in homosexuals, 10% in heterosexuals; transmission by venereal contact; in 1 study, 45% of women and 30% of men whose sexual partners had *Chlamydia* were infected; 60-70% of infants exposed at birth develop respiratory infection or chlamydial ophthalmia; incubation period 7-21 d

Agents: 30-40% *Ureaplasma urealyticum*, 28% *Mycoplasma genitalium,* 15-55% *Chlamydia trachomatis*, 8% *Haemophilus parainfluenzae*, 2% *Haemophilus influenzae*; *Bacteroides*, *Porphyromonas asaccharalytica, Prevotella melaninogenica,* anaerobic cocci, *Acinetobacter*, *Staphylococcus aureus*, *Moraxella catarrhalis*, other bacteria in association with urinary tract infection, acute prostatitis, urethral stricture or following instrumentation; *Trichomonas vaginalis* (usually asymptomatic in male), *Candida* (uncommon cause in male), *humanherpesvirus*; *Entamoeba histolytica* described in homosexual males; also trauma

Diagnosis: often asymptomatic; women: vaginal discharge, pain on urination, spotting after sexual intercourse, lower abdominal pain; men: mucopurulent or purulent urethral discharge, dysuria; pyuria (> 10 polymorphs/hpf in sediment from first few mL of freshly voided specimen); Gram stain (> 5 polymorphs per oil immersion field) and culture of urethral swab; leucocyte esterase test on first void urine

Chlamydia:

Males: can cause urethritis and epididymitis; urethral swabs or first void urine specimens may be used for immunofluorescence (sensitivity 40-75%), ELISA ((sensitivity 40-75%), PCR (sensitivity > 90%), DNA probe (sensitivity 40-75%), ligase chain reaction (sensitivity > 90%) or culture (sensitivity 50-90%)

Females: 9% of sexually active women under 25 infected; can cause endometritis, cervicitis, Bartholinitis, premature rupture of membranes and preterm delivery; all women 19-24 y and women > 24 y with new partner or multiple partners should be screened annually; cervical swab culture and direct immunofluorescence or ELISA; sensitivity is 70-96% for direct immunofluorescence and 60-96% for ELISA; specimens must contain mucosal epithelial cells (ie., columnar, not squamous); specimens for immunofluorescence may be refrigerated if read within 24 h, must be frozen if not read within 24 hours, and diagnosis should be based on the presence of elementary bodies only, reticular bodies being indistinguishable from bacteria; specimens for immunoassay keep at room temperature for up to 7 d; specificity for both these procedures is 94-99%; culture (McCoy cells or Cellmatics™) is more sensitive than either procedure if urethral swabs are used but gives low yields from urine; iodine staining and immunofluorescence of isolates are equivalent; all these methods are being supplanted by PCR (sensitivity 90%, specificity 99.8%) or ligase chain reaction; VIDAS ELFA also used (sensitivity 71%, specificity 100%, PVP 100%, PVN 98.5%); DNA probe also available; complement fixation test detects antibody to both *Chlamydia trachomatis* and *Chlamydia psittaci*

Treatment:

Chlamydia trachomatis: azithromycin 1 g orally as a single dose, doxycycline 100 mg orally 12 hourly for 7 d, tetracycline 500 mg orally 4 times daily for 7 d, erythromycin base or equivalent salt 500 mg orally 6 hourly for 7 d (can be used in pregnancy), sulphisoxazole or equivalent 500 mg orally 4 times daily for 10 d, ofloxacin 300 mg twice a day for 7 d, levofloxacin 500 mg once daily for 7 d; rescreen 3-4 mo after treatment

***Haemophilus*:** amoxycillin 500 mg orally 8 hourly for 5 d, erythromycin 500 mg orally 4 times daily for 7 d, amoxycillin-clavulanate 500/125 mg orally 8 hourly for 8 d

***Ureaplasma urealyticum*:** erythromycin 500 mg orally 8 hourly for 7 days, minocycline 100 mg orally 12 hourly for 7 days

Mycoplasma genitalium: azithromycin

Treatment Failure: metronidazole 2 g orally in a single dose + erythromycin base 500 mg orally 4 times a day for 7 d or erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 d

Prevention and Control: exposure prevention, treatment of cases

URETHRAL DISCHARGE occurs in 99% of cases of gonococcal urethritis (63% scanty, 78% yellow-green), 95% of non-gonococcal urethritis (96% scanty, 66% clear; *Haemophilus influenzae*: 40% moderate, 40% profuse, 60% clear; *Haemophilus parainfluenzae*: 47% moderate, 88% clear), and in acute epididymitis, acute prostatitis and prostatic abscess

PROSTATITIS AND SEMINAL VESICULITIS: may need to be considered as the cause of protein, mucus and neutrophils (and sometimes bacteria) in urine of males; patients may have relapsing urinary tract infections

Agents: *Neisseria gonorrhoeae*, *Escherichia coli* and other Enterobacteriaceae, *Staphylococcus saprophyticus, Mycobacterium avium-intracellulare* (rare; granulomatous), *Haemophilus parainfluenzae*, *Ureaplasma urealyticum, Candida albicans* and *Aspergillus* (uncommon cases in hemotologic malignancies, diabetes, corticosteroid use, AIDS), *Trichomonas vaginalis*

Diagnosis:

Acute: lower urinary tract symptoms + fever, systemic symptoms, perineal pain, exquisite tenderness of prostate

Chronic: little inflammation, prostate normal on examination; may be recurrent UTIs

culture of semen; quantitative counts of urine, comparing initial voided urine with midstream urine with urine after prostatic massage (or, preferably, ejaculate); semen acid phosphatase elevated for day or more following prostatic massage (in absence of prostatic carcinoma); white cell count usually elevated with neutrophilia

Treatment:

***Mycobacterium avium-intracellulare*:** ethambutol 15 mg/kg orally daily or 25 mg/kg orally 3 times weekly (not < 6 y) + clarithromycin 12.5 mg/g to 500 mg orally 12 hourly daily or 3 times weekly or azithromycin 10 mg/kg to 500 mg orally daily or 10 mg/kg to 600 mg orally 3 times weekly + rifampicin 10 mg/kg to 600 mg orally daily or 3 times weekly or rifabutin 5 mg/kg to 300 mg orally daily

Other Bacteria:

Severe Acute: amoxy(ampi)cillin 2 g i.v. 6 hourly + gentamicin 4-6 mg/kg (adjust dose for renal function) i.v. daily

Less Severe: cotrimoxazole 160/800 mg orally 12 hourly for 5 days; trimethoprim 240 mg orally daily initially then 80 mg orally daily + rifampicin 900 mg daily initially then 300 mg orally daily; minocycline 200 mg orally initially followed by 100 mg orally 12 hourly; norfloxacin 800 mg/d for 5 d

Chronic: norfloxacin 400 mg orally 12 hourly for 4 w, ciprofloxacin 500 mg orally 12 hourly for 4 w, trimethoprim 300 mg orally daily for 4 w, doxycycline 100 mg orally 12 hourly for 2-4 w

No Organism Isolated: erythromycin 500 mg orally 6 hourly, doxycycline 100 mg orally 12 hourly

Fungi: amphotericin B ± flucytosine; prostatic resection

Trichomonas vaginalis: metronidazole, tinidazole

Prophylaxis (*Mycobacterium avium* complex in HIV/AIDS; CD4 count < 50/µL): azithromycin 1.2 g orally weeekly, clarithromycin 500 mg orally 12 hourly, rifabutin 300 mg orally daily

Prostatic Abscess

Agents: *Staphylococcus aureus* (in younger patients without urinary obstruction), *Escherichia coli* and other Gram negative bacilli (in older patients with prostatic hypertrophy and urinary obstruction), *Candida albicans* (in catheterised diabetics receiving broad spectrum antibiotics), *Neisseria gonorrhoeae*, anaerobes, *Mycobacterium* (rare cases), *Burkholderia pseudomallei* (in 18% of male melioidosis cases)

Diagnosis: pus and bacteria in urine; computerised tomography of pelvis or transrectal ultrasonography; culture of abscess fluid; white cell count usually increased

Treatment: perineal needle drainage or transurethral incision and drainage +:

***Neisseria gonorrhoeae*:** ciprofloxacin

Burkolderia pseudomallei: ceftazidime 2 g i.v. 6 hourly or imipenem 1 g i.v. every 8 h for 2 w, then double strength cotrimoxazole twice daily for at least 3 mo (amoxycillin-clavulanate, doxycycline or fluoroquinolones if unable to tolerate sulphonamides)

Other Bacteria: cotrimoxazole

***Candida albicans*:** amphotericin B

Acute Epididymitis and Epididymoorchitis: 0.02% of new episodes of illness in UK

Agents: *Neisseria gonorrhoeae* (22% of cases in heterosexual men, rare in homosexual men), *Chlamydia trachomatis* (46% of cases in heterosexual men, rare in homosexual men), *Escherichia coli* and *Klebsiella pneumoniae* (67% of cases in homosexual men, rare in heterosexual men < 35 y, usual cause in children and heterosexual men > 35 y), *Haemophilus influenzae* (11% of cases in homosexual men, rare in heterosexual men; 5% of cases of non-bacteremic invasive *Haemophilus influenzae* infections in older children and adults), *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus*, *Salmonella*, *Treponema pallidum*, *Mycobacterium tuberculosis*, *Brucella* (in 5-9% of brucellosis cases), *Neisseria meningitidis*, *human cytomegalovirus* (in AIDS)

Diagnosis: swelling in 100%, pain in 96%, erythema in 72%, temperature > 37.7° in 40%; white cell count > 10,000/µL in 44%; cloudy urine; Gram stain, immunofluorescence and culture of aspirate, urine, urethral discharge; PCR for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* on intraurethral swab or first void urine; blood and stool cultures; serology; exclude urinary tract infection, testicular torsion

Treatment: infiltration of spermatic cord above testicle with procaine hydrochloride +:

Sexually Acquired: ceftriaxone 250 mg i.m. single dose + doxycycline 100 mg orally twice a day or roxithromycin 300 mg orally daily for 14 d; amoxycillin/clavulanate 500 mg orally 8 hourly for 10-14 d or ciprofloxacin 500 mg orally 12 hourly for 10-14 d or amoxycillin 500 mg orally 8 hourly for 10-14 d + doxycycline 100 mg orally 12 hourly 10-14 d

Associated with Urinary Tract Infection:

Mild to Moderate: trimethoprim 6 mg/kg to 300 mg orally daily for 14 d, cephalexin 12.5 mg/kg to 500 mg orally 12 hourly for 14 d, amoxycillin-clavulanate 12.5/3.1 mg/kg to 500/125 mg orally 12 hourly for 14 d, norfloxacin 400 mg orally 12 hourly for 14 d

Severe: amoxy(ampi)cillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin (< 10 y: 7.5 mg/kg; ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function) till substantial clinical improvement then appropriate oral agent to complete 14 d course; ofloxacin 300 mg orally twice a day for 10 d; levofloxacin 500 mg orally once daily for 10 d

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Pseudomonas aeruginosa: gentamicin + ticarcillin

Salmonella: cotrimoxazole 160/800 mg orally 12 hourly

ORCHITIS

Agents: mumps (usually unilateral; in 20-38% of postpubertal males with mumps), coxsackievirus B, Rocky Mountain spotted fever (in 1% of infections), *Salmonella* (in renal transplant recipients), *Chlamydia trachomatis*

Diagnosis: proteinuria; white cell count may be elevated; serology

Treatment: infiltration of spermatic cord just above testis with procaine hydrochloride

Salmonella: cotrimoxazole 160/800 mg orally 12 hourly

Chlamydia trachomatis: doxycycline

BARTHOLINITIS

Agents: wide variety of aerobic and anaerobic bacteria, mycobacteria, *Chlamydia*, fungi, parasites and viruses

Diagnosis: clinical; swab culture

Treatment: dependent on agent

VULVITIS

Agents: *Candida albicans*, *Simplexvirus*

Diagnosis and Treatment: see **VAGINITIS**, **GENITAL HERPES**

VAGINITIS: conditions involving actual infections which of themselves may cause discharge and other symptoms

Agents: *Neisseria gonorrhoeae* (prevalence 0-4/1000), *Chlamydia trachomatis* (21% of female sexually transmitted disease), *Trichomonas vaginalis* (worldwide; 19% of female sexually transmitted disease; up to 85% of female sexual partners of infected men infected; 30-40% of male partners of infected women infected; about 5% of girls born to infected women infected at birth; may also be transmitted at gynecological examination; incubation period 3-28 d; 5 M cases/y in USA; prevalence 32-70/1000; amplifies HIV transmission), *human herpesvirus* 2 (occasionally *human herpesvirus* 1), *Candida albicans* and other *Candida* species (11% of female sexually transmitted disease; prevalence 36-93/1000; 15-20% *C.glabrata*), *Saccharomyces cerevisiae*, *Haemophilus influenzae*, ? *Mycoplasma hominis*, ? echovirus 4, *Balantidium coli* (extremely rare)

Prepubertal Girls and Elderly Women: *Staphylococcus aureus*, *Streptococcus pyogenes*, other β-streptococci, coliforms, fecal streptococci, *Haemophilus influenzae, Actinomyces pyogenes*

Infant Girls: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Enterobius vermicularis*

Diagnosis: symptoms and signs have little value (vaginal discharge in candidiasis varies from clear and watery to creamy or cottage cheese-like, and occurs in only 55% of trichomoniasis cases, 69% of such discharges being non-frothy leucorrhoea and 12% frothy leucorrhoea); however, a foul odour is more likely to be associated with *Trichomonas vaginalis* or nonspecific or foreign body vaginitis, pruritus is usually intense in *Candida* infections, mild with *Trichomonas vaginalis* and absent or minimal in other conditions, and inflammation is usually intense in candidiasis, obvious in trichomoniasis and minimal in atrophic and foreign body states; pH 5.5-6.0 with *Trichomonas vaginalis*, < 4.5 with *Candida albicans*; wet preparation (motile trichomonads, yeasts, pseudomycelium; using phase contrast, even non-motile trichomonads can be detected, with sensitivity equal to that of culture; sensitivity of ordinary wet mount is only 60%; that of cytology is even

less at 55%), Gram stain and culture of vaginal pool found in posterior fornix when patient is in lithotomy position; direct immunofluorescence for *Trichomonas vaginalis* (sensitivity 86%, specificity 99%, PVP 96%, PVN 98%); serology; sticky tape preparation of anal area (children)

Recurrent Candidiasis: associated with pregnancy, uncontrolled diabetes mellitus, estrogens, corticosteroids, ? oral contraceptives, antibiotics, tight-fitting and synthetic clothing (panty hose, underwear), local allergy (commercial douches, perfumes), idiopathic, acquired antigen-specific immunodeficiency (cell-mediated immunity), AIDS, resistance of organism to antimycotic agents, ? switching colonies; culture of swabs from urethra, rectum, fingernails, throat, perineum; skin test; RAST

Treatment:

***Neisseria gonorrhoeae*:**

β-lactamase Negative: amoxycillin 3 g orally as single dose + probenecid 1 g orally as single dose + azithromycin 1 g orally as a single dose or doxycycline 100 mg orally 12 hourly for at least 10 d (pregnant or breastfeeding: erythromycin 500 mg orally twice daily or roxithromycin 300 mg orally once daily for at least 10 d)

β-lactamase Positive or Penicillin Hypersensitive: ceftriaxone 250 mg in 1% lignocaine hydrochloride i.m. as a single dose or spectinomycin 2 g i.m. as a single dose + azithromycin or doxycycline as above (pregnancy or breastfeeding: erythromycin or roxithromycin as above)

***Chlamydia trachomatis*, *Mycoplasma hominis*:**

Preadolescent Girls: consider sexual abuse as possible cause of chlamydial infection

≤ 45 kg: erythromycin base or ethylsuccinate 50 mg/kg/d orally in 4 divided doses for 14 d

≥ 45 kg but < 8 y: azithromycin 1g orally in single dose

≥ 8 y: azithromycin 1 g orally in single dose, doxycycline 100 mg orally twice a day for 7 d

Pregnant or Breastfeeding: erythromycin base 500 mg orally 4 times daily for 7 d or 250 mg orally 4 times daily for 14 d, amoxycillin 500 mg orally 3 times daily for 7 d, erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 d or 400 mg orally 4 times a day for 14 d, roxithromycin 300 mg orally once daily for 10-14 d

Others: azithromycin 1 g orally as a single dose, doxycycline 100 mg orally 12 hourly for 7-10 d, erythromycin base 500 mg orally 4 times daily for 7 d, erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 d

Streptococci: phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly for 7 d

Other Bacteria: tetracycline; triple sulpha cream at night

Candida glabrata, Saccharomyces cerevisiae: boric acid 600 mg in gelatin capsule intravaginally 10-14 d (not pregnant), flucytosine

Other *Candida*: butoconazole 2% cream 5 g intravaginally for 3 d or sustained release 2% cream 5 g single intravaginal application, intravaginal clotrimazole 500 mg pessary once only or 100 mg pessary 2 each night for 3 nights or 1 each night for 6 nights or 1% cream 5g nightly for 6 nights or 2% vaginal cream 1 applicator full for 3 nights or 10% vaginal cream 1 applicator full as single dose at night, miconazole nitrate 2% vaginal cream 5 g nightly for 7 nights or 200 mg vaginal suppository nightly for 3 nights, nystatin 100 000 U pessary or 100 000 U/5 g cream 1 applicatorful inserted high into vagina 12 hourly for 7 d, tioconazole 6.5% ointment 5 g intravaginally once, terconazole 0.4% cream 5 g intravaginally for 7 d or 0.8% cream 5 g intravaginally for 3 d or 80 mg vaginal suppository 1 nightly for 3 nights, fluconazole 150 mg orally single dose (not pregnant); ± clotrimazole 1% cream to vulvovaginal and perianal areas

Recurring or Unresponsive: clotrimazole 500 mg vaginal tablet inserted high into vagina at night, then weekly for 6 mo; fluconazole 50 mg orally daily, then 150-300 mg orally weekly; itraconazole 100 mg orally daily, then 100-200 mg orally weekly; nystatin 100 000 U/5 g vaginal cream 1 applicatorful or 100 000 U pessary intravaginally weekly

Male Partner: nystatin cream locally for 14 d

Multisite Carriage: oral ketoconazole

Hypersensitisation: desensitisation

Anergy: hyperimmune *Candida* transfer factor

***Trichomonas vaginalis*:**

Nonlactating Adults: metronidazole 2 g single oral dose, tinidazole 2 g orally single dose with food, nimorazole 250 mg orally twice a day for 3 d or 2 g single oral dose

Relapse: metronidazole 400 mg orally 12 hourly for 5 d

Lactating Women: interrupt breastfeeding for 24 h after giving metronidazole 2 g orally as a single dose

Children: metronidazole (< 3 y: 1/6 dose; 3-7 y: ¼ dose; 7-12 years: ½ dose)

***Simplexvirus*:** famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

***Enterobius vermicularis*:** pyrvinium embonate

VAGINOSIS: conditions in which diminution in numbers of protective hydrogen peroxide-producing Lactobacilli, with excessive overgrowth of endogenous flora, occurs due to physiological or local factors (eg. hormonal effects, sex, douching, IUD, use of some local preparations); associated complications include increased risk of HIV, recurrent cystitis, pelvic inflammatory disease (including post-abortion and subclinical), cervicitis, abnormal Papanicolaou smears, postsurgical gynecologic infections, early spontaneous abortion, miscarriage after 13 weeks, preterm labour, premature rupture of membranes, chorioamnionitis, postpartum endometritis

Agents: *Prevotella, Peptostreptococcus, Bacteroides, Eubacterium, Gardnerella vaginalis*, *Mobiluncus, Mycoplasma hominis,* enterococcus, *Streptococcus agalactiae*

Diagnosis: coaty, homogenous, white, non-inflammatory vaginal discharge, pH > 4.5, amine odour with 10% KOH; Gram stain (clue cells with few, or no, lactobacilli) and culture of vaginal swab; DNA probe-based test; card test for detection of elevated pH and trimethylamine; prolineaminopeptidase card test

Treatment: metronidazole 400 mg orally 12 hourly for 7 d, tinidazole 500 mg orally daily for 7 d, nimorazole 250 mg orally twice daily for 3 d, metronidazole gel 0.75% 5 g intravaginally once a day for 5 d, clindamycin phosphate 2% vaginal cream 5 g intravaginally at bedtime for 7 nights, clindamycin 300 mg orally twice a day for 7 d, clindamycin ovules 100 g intravaginally once at bedtime for 3 d; restoration of acid pH with Acigel™ etc

Pregnancy: treatment in early pregnancy reduces preterm birth by 60%; clindamycin 300 mg orally twice daily for 7 d, metronidazole 400 mg orally 12 hourly for 7 d

VAGINAL DISCHARGE also occurs in 28% of cases of *Staphylococcus saprophyticus* urinary tract infection. Nonvenereal vaginal discharge is responsible for 0.7% of new episodes of illness in the UK. Non-infective causes include cervical ectropion; pregnancy; estrogen deficiency (atrophic vaginitis); inflammation due to douches, deodorants, bath salts, perfumes, etc. Syphilis may also present with vaginal discharge.

GENITAL TRACT LISTERIOSIS: usually inapparent disease of genital tract; may be transmitted from pregnant female to offspring either transplacentally or by contact with infected secretions during delivery; hospital infections not uncommon and probably transmitted via hands of nurse

Agent: *Listeria monocytogenes*

Diagnosis: culture of vaginal swab

Treatment: amoxycillin/ampicillin

MUCOPURULENT CERVICITIS

Agents: *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma hominis*, *Trichomonas vaginalis*, *Candida albicans*

Diagnosis: Gram stain and culture of cervical swab; direct immunofluorescence (*Chlamydia*) of cytobrush (nonpregnant) or swab

Treatment: see **VAGINITIS**

NONPURULENT CERVICITIS

Agent: *human herpesvirus* 2, *human adenovirus 37*; *human cytomegalovirus* in AIDS

Diagnosis: viral culture and immunofluorescent stain of cervical swab

Treatment (*human herpesvirus 2*): famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

CERVICAL CARCINOMA: associated with sexual promiscuity (early coitus and multiple sexual partners)

Agent: certain strains of human papillomavirus (HPV-16, HPV-18)

Diagnosis (HPV-16, HPV-18): real time PCR

SALPINGITIS: 0.03% of new episodes of illness in UK

Agents: *Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma hominis, Campylobacter fetus* subsp *fetus, Escherichia coli, Bacteroides capillosus, Bacteroides putredinis, Prevotella disiens, Actinomyces israelii*

Diagnosis: clinical; Gram stain and culture of endocervical swab, culdocentesis material, material taken at operation; leucocytosis (white cell count > 10,000/μL); ultrasound (pelvic abscess or inflammatory complex)
Treatment: doxycycline + benzylpenicillin

TUBO-OVARIAN ABSCESS

Agents: 37% *Escherichia coli*, 22% *Bacteroides fragilis*, 26% other *Bacteroides* species, 19% aerobic streptococci, 17% *Peptostreptococcus,* 11% *Peptococcus,* 7% *Neisseria gonorrhoeae*
Diagnosis: clinical and physical examination; ultrasonography; laparoscopy or laparotomy; culture of needle aspirate or surgical specimen; white cell count > 10,000/μL in 75% of cases
Treatment: benzylpenicillin 20 M U/d i.v. in 4 divided doses + gentamicin 3-5 mg/kg/d i.v. in 3 divided doses + clindamycin 2.4 g/d i.v. in 4 divided doses; surgery

OOPHORITIS

Agents: mumps virus, varicella
Diagnosis: serology
Treatment: nonspecific

PERIHEPATITIS

Agents: *Neisseria gonorrhoeae, Chlamydia trachomatis*
Diagnosis: culture and immunofluorescence of cervical, urethral and rectal swabs; serology; laparoscopy
Treatment: doxycycline + benzylpenicillin

RAPE: gonorrhoea in 2-28% of victims, syphilis in < 1%, *Chlamydia* in 3-16%, *Trichomonas* in 6-27%, bacterial vaginosis in 12-20%
Investigations: history; physical examination of external genitals, of vaginal aspirate in female children presenting solely because of behavioural symptoms and with no genital abnormalities on external examination, of oral and anal mucosa (evaluate men for relaxed external sphincter, anal fissures and hemorrhoids, ascertain condition of prostate gland and perform proctoscopy if anorectal injury present or infection suspected); complete speculum and bimanual examination in women and female children if external examination shows any genital abnormality or if there is a history of recent vaginal penetration or if child presents with genital symptoms alone rather than with a history of sexual assault (general anesthesia may be necessary); culture or nucleic amplification test (confirm with second nucleic acid amplification test targeting different sequence if positive) for *Neisseria gonorrhoeae* and *Chlamydia* from any sites of penetration or attempted penetration, wet preparation and culture of vaginal swab for *Trichomonas vaginalis,* bacterial vaginosis and candidiasis; serology for syphilis, HIV and hepatitis B
Prophylaxis: if assailant is infected, victim is unlikely to return for follow-up or has signs or symptoms of infection, assault by a stranger, or prophylaxis requested by victim; ceftriaxone 250 mg (child: 125 mg) i.v. or i.m. as single dose (spectinomycin 40 mg/kg to 2 g i.m. if allergic to cephalosporins) + azithromycin 20 mg/kg to 1 g orally single dose + metronidazole 30 mg/kg to 2 g orally single dose or tinidazole 50 mg/kg to 2 g orally single dose; hepatitis B vaccine if unvaccinated + hepatitis B immunoglobulin if assailant known to be infected; HIV prophylaxis if unprotected receptive or insertive anal or vaginal intercourse and assailant known or suspected infected (consult HIV physician)
Follow-up: after 7 d, above tests less syphilis serology; after 6 w, syphilis serology

GENITAL ULCERATION

Agents: *Treponema pallidum, Haemophilus ducreyi, simplexvirus*, *Chlamydia trachomatis*, *Calymmatobacterium granulomatis*
Diagnosis and Treatment: serology and darkfield examination or direct immunofluorescence test for *T.pallidum,* culture or antigen test for *simplexvirus*, culture for *Haemophilus ducreyi;* see **SYPHILIS**, **CHANCROID**, **GENITAL HERPES**, **CHLAMYDIAL LYMPHOGRANULOMA, GRANULOMA INGUINALE**

SYPHILIS: a treponematosis; three forms recognised: acquired syphilis, congenital syphilis and nonvenereal syphilis

ACQUIRED SYPHILIS (GREAT POX, LUES, LUES VENEREA, MORBUS GALLICUS, ST JOB DISEASE, ST SEMENT DISEASE): worldwide; ≈ 2000 notified cases/y in Australia (≈ 42% in Queensland); incidence in USA 2.2/100,000; 3% of male sexually transmitted disease, 2% of female; 15% incidence in homosexuals; transmission by intimate contact with infectious exudates, almost exclusively during sexual contact; 30-60% of sexual partners become infected after 1 exposure; may pass through the placenta as early as ninth week of pregnancy in 2/3 or more of pregnancies, causing spontaneous abortion, stillbirth or neonatal death in 40% of cases; incubation period 10-90 d (mean 21 d); manifested in 3 stages: primary syphilis, secondary syphilis, tertiary syphilis; for public health purposes, it is convenient to classify cases either as early syphilis (covering both primary and secondary stages) or late syphilis
Agent: *Treponema pallidum subsp pallidum*
Diagnosis:

Primary: the initial stage, during which widespread dissemination of *Treponema pallidum* occurs; history of sexual contact often of doubtful reliability; only clinical manifestations are the chancre (dry papule, hard chancre, hard sore, hard ulcer, Hunter chancre, hunterian chancre, primary syphilitic sore, ulcus durum, ulcus induratum)—a hard lesion or painless ulcer on genitalia, perianal area, pharynx, tongue, lips appearing 10-90 d after infection and usually healing spontaneously in 4-6 w—and nontender, rather firm, unilateral regional lymphadenitis (primary syphilitic lymphadenitis); every lump, ulcer or fissure on, in or near the genitalia or anus should be suspected as being possibly primary syphilis; dark ground illumination and direct immunofluorescence of tissue fluid from chancre 3-4 w post-infection; TPHA or ELISA (sensitivity 97-100%, specificity 99.5-100%), quantitative RPR if positive, FTA-ABS if negative and clinical suspicion (all may be negative in AIDS); Western blotting; PCR or ligase chain reaction of lesion, tissue, CSF, blood

Secondary: begins at end of primary syphilis and lasts a few weeks to a year of more; principal manifestations a wide variety of skin lesions—macular, papular, maculopapular, pustular, ulcerative, follicular or nodular rash (syphilids), mucous patches (highly infectious lesions of a mucous membrane; 'snail-track ulcers'), condylomata lata (pale-coloured raised papular lesions, often with a flat surface, most frequently in genital and anal areas)—in ≈ 90%; generalised lymphadenopathy (diffuse, rubbery, symmetric, painless, small inguinal, posterior cervical, occipital, axillary, epitrochlear) in ≈ 85%; headache, fever, arthralgias, sore throat, rhinitis, tearing in ≈ 70%; rare meningismus, aseptic meningitis, cranial nerve involvement, oculopathy (cyclitis, iritis, choroiditis, retinitis), visceral (hepatitis, pericholangitis, mild nephrotic syndrome, rarely hemorrhagic nephritis), osteochondropathy (usually periostitis of long bones), myositis; any anogenital lump, generalised rash, mouth ulcer, alopecia or generalised lymphadenopathy should be suspected as being possibly due to secondary syphilis; dark ground examination of mucosal or cutaneous lesion; positive VDRL (99% positive) in the presence of positive FTA-ABS (99% positive) or TPHA (96% positive)

Latent: no physical signs; history of syphilis inadequately treated; positive FTA-ABS (96-99% positive) or TPHA (≈ 95% positive); VDRL positive for ≈ 75%; CSF negative

Recurrent Secondary Syphilis (Recurring Secondary Syphilis, Secondary Syphilitic Relapse): secondary syphilis, of any form, recurring after a period (of any duration) of latent syphilis

Late (Tertiary): not infectious; 25% of untreated patients asymptomatic (elevated protein, pleocytosis, positive serology of CSF); 6% symptomatic neurosyphilis (5-10 y: neurolues—meningovascular neurosyphilis, characterised by obliterative endarteritis, may cause syphilitic hydrocephalus, meningoencephalitis, seizures, stroke, transverse myelitis; 15-20 y: general paresis (cerebral tabes, syphilitic meningoencephalitis, dementia paralytica, general paralysis of the insane, general progressive paralysis, paralytic dementia, paretic dementia)—generalised meningoencephalitis as a manifestation of neurosyphilis, leading to fibrosis of meninges and atrophy of the brain with ultimately dementia and paralysis; 25-30 y: tabes dorsalis (locomotor ataxia, posterior sclerosis, syphilitic posterior spinal sclerosis, tabetic neurosyphilis)—degeneration of posterior column of spinal cord as a late manifestation of neurosyphilis, complications including Charcot joint resulting from neurotrophic disturbances, and severe gastric functional disturbances with paroxysm ('gastric crisis'); neuritis arising as a manifestation of neurosyphilis most commonly affects the acoustic and optic nerves, the Argyll-Robertson pupil being a classic manifestation); 10% cardiovascular symptoms (mesaortitis with aortic aneurism as possible consequence, endocarditis, pericarditis, aortic valve insufficiency, aortic ectasia particularly ascending aorta, coronary artery stenosis); uncommonly cutaneous (one or more indolent nodules and/or gummata distributed symmetrically) or mucocutaneous; gummata may affect skin, mucous membrane, bone, soft tissue, almost any organ; osteochondropathy affecting cranial bones, tibia, clavicle, fingers, toes, causing bone pain, pathologic fractures, joint destruction, nasal septal and/or palatal perforation; myositis; visceral (most frequently hepatitis, nephropathy

Late Benign or Cardiovascular: positive FTA-ABS (97% positive) or TPHA (≈ 95% positive) on serum and a normal CSF examination

Neurosyphilis: CSF leucocyte count > 5/mm^3; VDRL on CSF (sensitivity 30-70%); if negative, microhemagglutination or FTA-ABS on CSF; if these positive, TPHA index, IgG TPHA ratio, quantitative MHA-TP

Treatment:

Primary, Secondary or Early Latent: benzathine penicillin G 37.5 mg/kg to 1.8 g i.m. as a single dose at once, giving ½ dose into each buttock, followed if possible by 1.8 g after 7 d; aqueous procaine penicillin 1 g i.m. daily for 10 d; treat all sexual contacts within last 3 mo even if RPR negative

Penicillin Hypersensitive: consider desensitisation; doxycycline 100 mg orally 12 hourly for 14 d (not pregnant or breastfeeding)

Human Immunodeficiency Virus Infected Patients: benzylpenicillin 2.4 MU i.v. 4 hourly for 10 d, aqueous procaine penicillin 2.4 MU i.m. daily + probenecid 500 mg orally 6 hourly

Late Latent: benzathine penicillin 37.5 mg/kg to 1.8 g i.m. once weekly for 3 w, procaine penicillin 1 g i.m. once daily for 15 d

Penicillin Hypersensitive: consider desensitisation; doxycycline 100 mg orally 12 hourly for 28 d (not pregnant or breastfeeding)

Tertiary: benzylpenicillin 1.8 g i.v. 4 hourly for 15 d

Cardiovascular Syphilis, Neurosyphilis: + prednisolone or prednisone 20 mg orally 12 hourly for 3 doses

Follow-up:

Primary: serology every 3 mo for 1 y

Secondary, Latent and Late: serology every 3 mo for 1 y, then at 18 and 24 mo

Prophylaxis (Exposure <30 d): procaine benzylpenicillin 2.4-4.8 MU i.m., ceftriaxone 125 mg single dose

Prevention and Control: exposure prevention, identification and treatment of cases

CONGENITAL SYPHILIS: see Chapter 5

NONVENEREAL SYPHILIS (BEJEL (EUPHRATES VALLEY), DICHUCHWA (BOTSWANA), ENDEMIC SYPHILIS, ENDEMIC SYPHILIS OF THE BEDOUINS, NJOVERA (ZIMBABWE), SITI (GAMBIA, SENEGAL), SKERLJEVO OR SKRLEVO (BOSNIA-HERZEGOVINA, MACEDONIA))

AGENT: *Treponema pallidum* subsp *endemicum*

Diagnosis: similar to **ACQUIRED SYPHILIS** except primary stage often passes unnoticed and more serious late manifestations are rare; all serological tests for syphilis positive; differential diagnosis from acquired syphilis only possible within epidemiological setting

Treatment: as for **ACQUIRED SYPHILIS**

CHANCROID (CHANCRELLE, CHANCRE MOU, CHANCRE SIMPLEX, DUCREY CHANCRE, DUCREY DISEASE, GENITAL ULCER, SIMPLE CHANCRE, SOFT CHANCRE, SOFT SORE, ULCUS MOLLE): worldwide; acute, sexually transmitted infectious disease of the genitalia; people infectious as long as they have ulcers; no transmission from mother to fetus or during delivery; rare cases in Australia; ≈ 700 cases/y in USA; incubation period 1-10 d (usually 3-7 d); found in 15% of primary syphilitic chancres and 28% of patients with herpes genitalis

Agent: *Haemophilus ducreyi*

Diagnosis: women may have no symptoms; 1 or more painful pustular lesions, at entrance to vagina and around anus in women and on penis in men, that may rupture to form suppurative ulcers; women may have pain on urination or defecation, rectal bleeding, pain on intercourse or vaginal discharge; regional lymphadenopathy (inguinal adenitis with softening appearing after 7-10 d) in up to ½ of cases; microscopy (characteristic arrangement of bacteria) and culture (high humidity at 33-35°C on enriched gonococcal agar + 1% bovine hemoglobin + 5% serum and on Muller-Hinton agar + 5% chocolatised horse blood, repeating culture on first medium at 48 h) of swab of lesion or aspirate from flocculant node (sensitivity 92%; negative cultures 38% prior medication, 38% syphilis, others ?); occasionally, a biopsy may be required; tests for syphilis and *simplexvirus* virus negative

Treatment (Patients and Sexual Partners): ulcers disappear without treatment usually in about a month but may last up to 12 w; azithromycin 1 g orally as single dose (not in pregnant or breastfeeding), ceftriaxone 250 mg i.m. as a single dose, ciprofloxacin 500 mg twice a day orally for 3 d (not in pregnant or lactating women), erythromycin 500 mg orally 8 hourly for 7 d, cotrimoxazole 160/800 mg orally 12 hourly for minimum 10 d, tetracycline 500 mg orally 6 hourly for 14-21 d, sulphisoxazole 1 g orally 6 hourly for 10 d, amoxycillin-clavulanate 500/125 mg 8 hourly for 7 d, rosoxacin 450 mg 12 hourly orally for 3 d; reexamine 3-7 d after initiation of therapy; incision and drainage of buboes if required

Prevention and Control: exposure prevention

GENITAL HERPES: 5% of sexually transmitted disease in male, 4% in female; 0.2-0.5 M cases/y in USA (20% seroprevalence in > 12 y old; 30% increase in past decade); 10% incidence in homosexuals; 30/100,000 physician's visits; 17% of women and 4% of men infected when living with infected partner for median 344 d; > 90% of persons with genital *simplexvirus* 2 shed virus asymptomatically; incubation period 1-26 d (average 6-7 d)

Agent: *simplexvirus* (up to 30% *simplexvirus* 1 (recurrences much less frequent), remainder *simplexvirus* 2)

Diagnosis: 60% unrecognised with symptoms, 20% recognised genital herpes, 20% truly asymptomatic; painful, multiple, blisterlike, ulcerating lesions in and around vagina, around anus or on thighs in women or on penis in men; can cause vulval/perianal fissures, internal lesions, reddening on buttocks/thighs, painful urination, vaginal/urethral discharge, aching lower limbs, headache, radicular or lower back pain, fever, malaise, stiff neck, abnormal sensitivity to light; may mimic cystitis, candidiasis or prostatitis; can lead to cervicitis and proctitis; ½ of those infected have recurrences, involving smaller and fewer lesions and less severe systemic reactions, though pain, numbness or tingling in buttocks, legs or hips may precede outbreak; immunofluorescence, viral culture (Cellmatics™ mink lung cells most useful cell line for

isolation and typing; if other viruses also sought, MRC-5 is probably the most suitable cell line; virus isolated from cervix in 70-90% of primary, but only 30-50% of recurrent, cases), Tzanck preparation (insensitive and nonspecific), ELISA (antigen and antibody; commercial systems inaccurate or misleading regarding virus type), PCR (100% specificity, greater sensitivity than culture), electron microscopy, Western immunoblot assay (type specific; sensitivity and specificity ≈ 100%), glycoprotein G-2 immunoblot assay (type specific; sensitivity 80-98%, specificity ≥ 96%)

Treatment: paint with povidone iodine 6 times daily for 7 d; famciclovir 500 mg orally 12 hourly for 5 d, valaciclovir 500 mg orally 12 hourly for 5 d, aciclovir 400 mg orally 8 hourly for 5 d (preferred in pregnancy); lignocaine 2% jelly may be used in first 24-36 h for pain relief

Infrequent, Severe Recurrences: commence at onset of prodromal symptoms or within 1 d of lesion onset; aciclovir 400 mg orally 8 hourly for 5 d (preferred in pregnancy), famciclovir 1 g orally for 1 d or 125 mg orally 12 hourly for 5 d or 500 mg orally 12 hourly for 7 d (in immunocompromised), valaciclovir 500 mg orally 12 hourly for 3 d

Frequent, Severe Recurrences: famiclovir 250 mg (500 mg in immunocompromised) orally 12 hourly for up to 6 mo, valaciclovir 500 mg orally 12 hourly (in immunocompromised) or 500 mg orally daily (< 10 recurrences per year on suppressive therapy) or 1 g orally daily (> 10 recurrences per year on immunosuppressive therapy) for up to 6 mo, aciclovir 200 mg (400 mg in late pregnancy) orally 1 hourly for up to 6 mo

Chlamydial Lymphogranuloma (Benign Inguinal Lymphogranulomatis, Climatic Bubo, Durrant-Nicholas-Farre Disease, Frei Disease, Inguinal Lymphogranulomatis, Lymphogranuloma inguinale, Lymphogranuloma Inguinalis, Lymphogranuloma Tropicum, Lymphogranuloma Venereum, Lymphoma Inguinale, Lymphomatosis Inguinales Suppurativa Subacuta, Lymphopathia Venerea, Lymphopathia Venereum, Nicholas-Farre Disease, Poradenitis Inguinalis, Poradenitis Nostras, Poradenitis Venerea, Poradenolymphitis, Poradenolymphitis Nostras, Poradenolymphitis Suppurativa, Suppurative Inguinal Adenitis, Tropical Bubo, Venereal Lymphogranuloma, Venereal Lymphopathy): principally tropical countries, including Australia (last notified case in 1995); incidence 0.09/100,000 in USA; < 1% of sexually transmitted disease; transmission by venereal contact; probably less transmissible than gonorrhoea; incubation period 3-12 d for genital lesion, 10-30 d for inguinal bubo

Agent: *Chlamydia trachomatis* L1-L3 serovars

Diagnosis: transient small papule (cutaneous or mucosal), subsequent slowly suppurating, tender inguinal and femoral buboes (most commonly unilateral) and lymphadenopathy, often with microabscess formation; women and homosexual men have no symptoms or lower abdominal or back pain, proctocolitis or inflammatory involvement of perirectal or perianal lymphatic tissues resulting in fistulas or strictures; 20-30% of women have inguinal buboes; systemic symptoms; anal intercourse may lead to rectal infection; 2/3 of buboes shrink and form fibrous masses, 1/3 rupture and leave scars; may be anorectal and/or vulvar lesions and genito-anorectal strictures (esthiomène) as a manifestation of chronic stage; prostatitis has been described as a subacute phenomenon; in 20%, inguinal lymph nodes separate from femoral lymph nodes to form inguinal groove; other sequelae include fistula, chronic inflammation of lymph nodes, cervicitis, urethritis and enlargement of genitalia; cytology and microimmunofluorescence of pus or biopsy; serology (complement fixation titres ≥ 1:64); dark ground illumination, tests for *Haemophilus ducreyi* and acid-fast bacilli negative; skin test (Frei test); white cell count 20,000/μL

Treatment: doxycycline 100 mg orally twice daily for 21 d (not in pregnant or breastfeeding), roxithromycin 300 mg orally daily for 21 d, azithromycin 1 g orally weekly for 3 w (not in pregnant or breastfeeding), erythromycin 30 mg/kg to 500 mg 4 times a day for 21 d; aspiration of infected buboes; surgical treatment of strictures

Prevention and Control: exposure prevention, treatment of cases

Granuloma Inguinale (Chronic Venereal Sores, Donovaniasis, Donovaniosis, Fifth Venereal Disease, Granuloma Contagiosa, Granuloma Genito-inguinale, Granuloma Inguinale Tropicum, Granuloma Pudendi, Granuloma Pudendi Tropicum, Granuloma Venereum, Granuloma Venereum Genito-inguinale, Infective Granuloma, Lupoid Form of Groin Ulceration, Pudendal Ulcer, Sclerosing Granuloma, Serpiginous Ulceration of the Genitals, Serpiginous Ulceration of the Groin, Ulcerating Granuloma of the Genitals, Ulcerating Granuloma of the Pudenda, Ulcerating Sclerosing Granuloma, Venereal Granuloma): a chronic mucocutaneous disease; endemic in India, Papua New Guinea, central Australia, southern Africa; 16 notified cases in Australia (tropical and near tropical areas) in 1999, showing steady decrease from 119 notified cases in 1994; incidence 0.02/100,000 in USA; usually transmitted by sexual contact; incubation period 8-80 d

Agent: *Klebsiella granulomatis*

Diagnosis: women may have no symptoms; painless, spreading, ulcerating, granulomatous lesions of genitalia (usually labia, prepuce or glans) and adjacent areas (extragenital lesions uncommon); lesion is covered by beefy-red granulation tissue and has raised-rolled, but not undermined, margins, and bleeds easily on contact; without treatment, may erode genitalia or block urethra; no regional lymphadenopathy; Giemsa stain of tissue scrapings from granuloma or aspirate from enlarged lymph glands ('Donovan bodies' seen in cytoplasm of mononuclear cells); precipitin and complement fixation tests
Treatment:

Not Pregnant or Breastfeeding: azithromycin 500 mg orally once daily for 7 d or 1 g orally once weekly for 4 w or until healing occurs, doxycycline 100 mg orally 12 hourly or 200 mg orally daily for 3-6 w, cotrimoxazole 160/800 mg orally 12 hourly for 3-6 w, chloramphenicol 500 mg orally 6 hourly for 2-6 w (average total dose required may reach 33.6 g in Papua New Guinea), gentamicin 1 mg/kg i.v. 8 hourly for up to 21 d, ciprofloxacin 750 mg orally 4 times a day for at least 3 w

Pregnant or Breastfeeding: erythromycin 500 mg orally 6 hourly for 3-6 w, roxithromycin 300 mg orally once daily for 2-6 w

Prevention and Control: exposure prevention

VENEREAL WARTS (CONDYLOMATA ACUMINATA): 20% incidence in homosexuals

Agent: human papillomavirus (types 6 and 11 > 90%)

Diagnosis: cytology

Treatment:

Vaginal: cryotherapy with liquid nitrogen; bichloroacetic acid or trichloroacetic acid 80-90% weekly

Urethral: cryotherapy with liquid nitrogen, podophyllin 10-25% in compound tincture of benzoin weekly

Anal: cryotherapy with liquid nitrogen, trichloracetic acid or bichloracetic acid 80-90% weekly, surgical removal

Oral: cryotherapy with liquid nitrogen, surgical removal

Others: podofilox 0.15% cream or 0.5% solution or gel topically twice daily for 3 consecutive days each week for 4-6 w until warts disappear (not pregnant or breastfeeding); imiquimod 5% cream topically once daily at bedtime and washed off after 6-10 h 3 times a week for up to 16 w (not pregnant or breastfeeding); cryotherapy repeated every 1-2 w until resolved; podophyllin resin 25% in compound tincture of benzoin topically and washed off after 6 h weekly until warts disappear (not pregnant); trichloroacetic acid or bichloroacetic acid 80-90% weekly; electrosurgery; surgical removal; intralesional interferon; laser surgery

Note: human papillomavirus 16 and 18 cause 70% of cervical cancers; they may be detected by PCR or dot-blot; 13 other high risk types cause the remainder; all high risk types can (uncommonly) cause penile intraepithelial neoplasia; types 16 and 18 also cause 25% of low-grade squamous intraepithelial lesions, while types 6 and 11 cause 5-25%; types 6 and 11 do not cause cervical cancer

ERYTHROPLASIA OF QUEYRAT: carcinoma in situ of penis

Agent: human papilloma virus 16

Diagnosis: cytology

Treatment: 5% imiquimod cream

MOLLUSCUM CONTAGIOSUM: benign cutaneous viral disease

Agent: *molluscum contagiosum virus* (poxvirus)

Diagnosis: cytology

Treatment: deroof aseptically with a needle or sharp pointed stick and express contents or treat as for warts

BALANITIS

Agents: superficial skin infection with *Staphylococcus aureus*, *Streptococcus pyogenes*; overgrowth of normal skin organisms due to poor hygiene; balanoposthitis due to *Candida*, *Bacteroides*, *Porphyromonas asaccharolytica, Prevotella melaninogenica,* anaerobic cocci, *Treponema* species other than *Treponema pallidum* subsp *pallidum* and *Treponema pallidum* subsp *pertenue* (may be acute ulcerative necrotising (Corbus disease, corrosive balanitis, erosive balanitis, fourth venereal disease, ulcerative balanoposthitis, venereal balanitis); severe tissue destruction may result and gangrene (balanitis gangrenosa, gangrenous balanitis, specific and ulcerative balanoposthitis) may occur), *simplexvirus*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*; circinate balanitis in Reiter's syndrome

Diagnosis: inflammation of the glans penis ± inflammation of prepuce; culture of swab

Treatment: cleaning with normal saline

***Candida*:** clotrimazole 1% + hydrocortisone 1% cream topically 12 hourly or miconazole 2% + hydrocortisone 1% topically twice daily for 2 w after symptoms resolve; screen for diabetes; consider circumcision in extreme recurrent relapsing

Sexually Transmitted Diseases: see relevant sections
Staphylococcus: di(flu)cloxacillin 12.5 mg/kg orally or i.v. 6 hourly for 5-7 d
Streptococcus pyogenes: phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly for 10 d
Other Bacteria: erythromycin orally 12 hourly for 5-7 d, roxithromycin orally once daily for 5-7 d

Chapter 5

Prenatal, Perinatal and Puerperal Infections

ABORTION

Agents: rubella, *human cytomegalovirus*, vaccinia, hepatitis B, Lassa fever virus, smallpox, varicella (20% mortality), *Listeria monocytogenes* (infection in first trimester found in Middle East, not in Western Europe, where infection in third trimester occurs), *Haemophilus influenzae*, *Campylobacter fetus* subsp *fetus*, *Campylobacter jejuni*, *Campylobacter coli, Leptospira, Streptococcus agalactiae, Coxiella burnetii, Streptococcus equinus*

Diagnosis: serology (complement fixation test, hemagglutination inhibition); bacterial and viral culture of saliva, gastric washings, urine, liver biopsy; post-mortem histology of salivary glands, adenoids, kidneys, liver, lymph glands, myocardium, spleen, pancreas, adrenals; serology

Prophylaxis:

***Listeria monocytogenes* in Pregnancy:** benzylpenicillin 15-20 MU i.v. daily in divided doses for 2 w ± gentamicin 1.3 mg/kg i.v. 8 hourly

Coxiella burnetii* in Pregnancy*: cotrimoxazole for duration of pregnancy

Rubella: mass immunisation of girls and boys; pre-pregnancy screening for rubella antibodies, followed by immunisation of susceptible women; antenatal screening for rubella antibodies, followed by post-partum immunisation of susceptible women

Varicella: live attenuated vaccine (44-85% effective; do not administer if pregnant)

STILLBIRTH

Agents: 14% parvovirus B19, rubella virus, *human cytomegalovirus*, hepatitis B, *Treponema pallidum*, *Toxoplasma gondii*, *Listeria monocytogenes, Campylobacter fetus* subsp *fetus*

Diagnosis: bacterial and viral culture of lymph nodes, lung, spleen, other tissues; serology (rubella: hemagglutination inhibition, complement fixation test)

Parvovirus B19: ELISA (IgM, IgG (kits using recombinant protein more sensitive and specific than those using a synthetic peptide)), PCR of maternal serum or amniotic fluid

Toxoplasma gondii: isolation from placenta, umbilical cord or infant blood; PCR of white blood cells, CSF or amniotic fluid (reference laboratory); IgM and IgA serology; IgG avidity (urea dissociable)

Prophylaxis:

***Listeria monocytogenes* in Pregnancy:** benzylpenicillin 15-20 MU i.v. daily in divided doses for 2 w ± gentamicin 1.3 mg/kg i.v. 8 hourly

Coxiella burnetii* in Pregnancy*: cotrimoxazole for duration of pregnancy

***Toxoplasma gondii* in Pregnancy:** spiramycin 3 g orally in divided doses

Rubella: see under **ABORTION**

Syphilis: routine antenatal screening and treatment of infected women

TERATOGENIC EFFECTS

Agents: rubella (transient common: intrauterine growth retardation, large anterior fontanelle; transient uncommon: cloudy cornea; permanent common: sensorineural deafness, spastic diplegia, patent ductus arteriosus, pulmonic stenosis, cataract and microphthalmia, retinopathy; permanent uncommon: glaucoma, inguinal hernia, cryptorchidism; permanent developmental common: central language disorders, mental retardation, behavioural disorders; permanent development uncommon: severe myopia), *human cytomegalovirus*, human immunodeficiency virus, lymphocytic choriomeningitis virus (from pet rodents)

Diagnosis: serology (rubella specific IgM present or infant's IgG titre does not fall off at expected rate of 1 doubling dilution per month); viral culture of throat swab and urine; ELISA, Western blot

Prophylaxis (Rubella): see under **ABORTION**

PRENATAL GENERALISED DISEASE

Agents: *human cytomegalovirus* (3-15% of pregnancies, 0.4-7% of live births; multisystem involvement (cytomegalic inclusion disease), usually a sequel of primary maternal infection; microcephaly, seizures, mental retardation, periventricular calcification, deafness (inner ear involvement), chorioretinitis, hepatosplenomegaly, jaundice, thrombocytopenia, petechial rash; sequelae in 90% of survivors—70% microcephaly, 60% mental

retardation; most disappear within 4 y, but 29% IQ < 90, 16% IQ < 80, 16% microcephaly, 12% bilateral hearing loss, 2% chorioretinitis), *simplexvirus* (5% of neonatal herpes, 1 in 300,000 deliveries; 10% risk if infection > 32 w gestation; if mother has first episode, 50% infected at birth; during recurrent episode, 3-5%; most transmission occurs while mother has no symptoms), rubella (0.1-4% of pregnancies, 0.05-3% of live births; transient common: thrombocytopenic purpura, hepatosplenomegaly, meningoencephalitis, bone lesions; transient uncommon: generalised adenopathy, hepatitis, hemolytic anemia, pneumonia, myocarditis), *Neisseria gonorrhoeae*, *Treponema pallidum* subsp *pallidum*, varicella-zoster (malformations, 18% disseminated infections), *Listeria monocytogenes* (neonatal disseminated listeriosis (disseminated infantile listeriosis, granulomatosis infantiseptica, listeriosis of the newborn) contracted transplacentally and widely distributed in the fetus, resulting in abortion, premature birth, stillbirth or death shortly after delivery), *Plasmodium, Candida* (low birth weight, pneumonia and skin rash), *Campylobacter fetus* subsp *fetus*, *Campylobacter jejuni*, *Toxoplasma gondii* (meningitis)

Diagnosis: cultures of blood and urine; Giemsa stain of blood film; demonstration of specific IgM antibody in cord or neonatal serum (hemagglutination inhibition, passive hemagglutination, immunofluorescence, ELISA); serology of CSF; viral culture of throat swab, saliva, gastric washings, urine

Congenital *Human cytomegalovirus* Disease: hepatomegaly in 100%, splenomegaly in 100%, mental retardation in 80%, microcephaly in 80%, motor disability in 75%, jaundice in 66%, petechiae in 55%, chorioretinitis in 30%, cerebral calcification in 25%; increased cord serum IgM in 85%, atypical lymphoctosis in 80%, increased SGOT in 80%, thrombocytopenia in 60%, increased bilirubin in 60%, increased CSF protein in 45%; viral culture positive at birth or within 1-2 w, characteristic inclusions seen on cytological examination of urine, IgG antibody; early marker of fetal infection is depression of cellular immunity in mother during pregnancy when exposed to primary *human cytomegalovirus* infection

Maternal Rubella Infection during Pregnancy: rising titres in hemagglutination and complement fixation tests; high titres of specific IgM

Congenital Malaria: platelet count 32,500/µL, serum bilirubin 4.1 mg/dL, white cell count 6900/µL, haematocrit 28%

Congenital Syphilis (Antenatal Syphilis, Foetal Syphilis, Prenatal Syphilis): syphilis arising in a neonate, infant or child as a result of intrauterine infection of fetus; fetus is infected transplacentally as early as the ninth to tenth week of gestation in 2/3 or more of pregnancies; incidence 13/100,000 live births in USA; CSF analysis for VDRL, cell count and protein; complete blood count, differential and platelet count; long bone radiographs; other tests as clinically indicated

Early (Not Before Third Week Postpartum in 80% of Infants): rhinitis (snuffles; early congenital/prenatal syphilitic coryza; obstruction and discharge—often bloody; one of most characteristic features of early congenital syphilis; severe cases may lead to permanent cracks or fissures (rhagades) about nose or mouth); laryngitis causing characteristic aphonic cry; often fatal pneumonia (early congenital syphilitic pneumonia, indurative syphilitic pneumonia of the newborn, pneumonia alba, primary congenital syphilitic pneumonia) in about 20% of cases, with diffuse interstitial fibrosis and fatty degeneration of lung parenchyma; bullae and vesicles; diffuse maculopapular or papulosquamous desquamative rash, most commonly on palmar, plantar, facial and anal areas; mucous patches; condylomata lata; osteitis (syphilitic osteitis of the newborn; nasal osteitis may cause destruction of vomer and saddle nose), osteomyelitis, periostitis (a hypertrophic, progressive condition affecting tibia leads to sabre shin), osteochrondritis (syphilitic osteochondritis of the newborn, Wegner disease, Wegner osteochondritis; femur and humerus most frequently affected; severe osteochondritis may lead to epiphysial separation, causing early congenital syphilitic paralysis—Bednar-Parrot disease, Parrot disease, Parrot pseudoparalysis, syphilitic pseudoparalysis), epiphysitis, chondroepiphysitis, perichondritis may be present at birth; hepatosplenomegaly; jaundice; thrombocytopenia, leucocytosis, anemia; paroxysmal cold hemoglobinuria; nephropathy (mild, acute nephritis, nephrotic syndrome or both); neurologic signs; lymphadenopathy

Latent Congenital Syphilis: serum is serologically positive and CSF negative and there are no symptoms

Late Congenital Syphilis (Syphilis Hereditaria Tarda): 2-30 y; interstitial keratitis gives cornea ground-glass appearance, becomes bilateral and leads to blindness; nerve deafness ('eight nerve deafness' affecting vestibulomandibular (eighth cranial) nerve); recurrent arthropathy (hydrarthosis; Clutton joint, Clutton syndrome; most frequently knee); odontopathy (notched incisors—Hutchinsonian teeth, Hutchinson's incisors, Huthinson teeth; domed front molars—Moon molars, Moon teeth; first molars with botryoidal occlusal surface—mulberry molars, mulberry teeth); frontal bosses a common result of hypertrophic periostitis; poor

maxillary development; protruding mandible; high palatal arch; rhagacles; thickening of inner part of right clavicle (clavicular sign, Higouménakis sign); flaring scapulas; neurosyphilis; gumma; (Hutchinson triad = congenital syphilitic keratitis with eighth nerve deafness and notched incisors); rising VDRL titre diagnostic; positive FTA-ABS-IgM suggestive but not diagnostic (10% false positive); negative FTA-ABS-IgM does not exclude diagnosis (35% false negative); results for both improved using 19S reagent; DFA Tp monoclonal; EIA IgM; immunoblot IgM of serum; PCR of serum or blood

Listeria monocytogenes: respiratory distress, vomiting, diarrhoea, maculopapular skin lesions, hepatosplenomegaly, meningitis; blood cultures, CSF examination

Toxoplasma gondii: mostly few symptoms at birth; later, generally develop mental retardation, severely impaired eyesight, cerebral palsy, seizures unless treated; isolation from placenta, umbilical cord or infant blood; PCR of white blood cells, CSF or amniotic fluid (reference laboratory); IgM and IgA serology; IgG avidity (urea dissociable) on mother in pregnancy

Herpes: scarring, active lesions, hypopigmentation, hyperpigmentation, aplasia cutis, erythematous macular exanthem, microophthalmia, retinal dysplasia, optic atrophy, chorioretinitis, microcephaly, encephalomalacia, hydranencephaly, intracranial calcification; PCR of CSF, blood

Treatment:

Gonorrhoea: benzylpenicillin 45-60 mg/kg i.v. daily in 4 divided doses for 7-10 d

Syphilis:

Mother Adequately Treated Before 28 w Gestation and Not Reinfected: benzathine penicillin 37.5mg/kg i.m. as a single dose

Not As Above or Symptoms Present: benzylpenicillin 50 mg/kg i.m. or i.v. 12 hourly for 10 d, procaine penicillin 50 mg/kg i.m. daily for 10 d

***Listeria monocytogenes*:** benzylpenicillin 50 000-1 MU daily i.v. for 2 w

***Candida*:** amphotericin B

***Simplexvirus*:** aciclovir

Rubella: none; consider abortion if infection detected during pregnancy

***Plasmodium*:** chloroquine

***Toxoplasma* (in Pregnancy):** spiramycin 3 g orally daily in divided doses + sulphadoxine-pyrimethamine 500/75 mg orally every 10 d + folinic acid; spiramycin 3 g orally in divided doses for 3 w, alternating with pyrimethamine-sulphadiazine 50 mg/3 g orally daily for 3 w + folinic acid

Prophylaxis:

***Listeria monocytogenes* in Pregnancy:** benzylpenicillin 15-20 MU i.v. daily in divided doses

Prevention and Control:

Rubella: mass immunisation of girls and boys; pre-pregnancy screening for rubella antibodies, followed by immunisation of susceptible women; antenatal screening for rubella, followed by postpartum immunisation of susceptible women

***Human cytomegalovirus*:** viral isolation from amniotic fluid

Syphilis: routine antenatal screening and treatment of infected women

Gonorrhoea: Gram stain and culture of cervical swab of pregnant women in population groups in which gonorrhoea is more common, with symptoms suggestive of gonococcal infection or in a high risk group for STD

Varicella: live attenuated vaccine (44-85% effective; do not administer if pregnant)

PERINATAL GENERALISED DISEASE: 25% of perinatal deaths

Agents: *Staphylococcus epidermidis* (16% of neonatal sepsis/meningitis), *Klebsiella pneumoniae* (15% of neonatal sepsis/meningitis), *Streptococcus agalactiae* (12-25% of neonatal sepsis/meningitis; early onset pneumonia, septicemia, late onset meningitis, endocarditis, abscess, myocarditis, osteomyelitis), *Escherichia coli* (10-16% of neonatal sepsis/meningitis), *Staphylococcus aureus* (7% of neonatal sepsis/meningitis), viridans streptococci (6% of neonatal sepsis/meningitis; *Streptococcus mitis* 0-5%), *Enterobacter cloacae* (5% of neonatal sepsis/meningitis), *Enterococcus* (4% of neonatal sepsis/meningitis), non-*Enterococcus* group D streptococci (3% of neonatal sepsis/meningitis), group C streptococci (0.6% of neonatal sepsis/meningitis), *Streptococcus milleri* (0-5% of neonatal sepsis/meningitis), other streptococci (2% of neonatal sepsis/meningitis), *Listeria monocytogenes* (2% of neonatal sepsis/meningitis), *Serratia marcescens* (2% of neonatal sepsis/meningitis), *Proteus* (2% of neonatal sepsis/meningitis), *Haemophilus influenzae* (nontypeable strains; 0.6-8% of neonatal sepsis/meningitis;

sepsis/respiratory distress syndrome; 83% early postnatal onset, 44-66% associated maternal complications, 83-88% premature, 50-90% mortality), *Corynebacterium* (0.6% of neonatal sepsis/meningitis), *Citrobacter* (0.6% of neonatal sepsis/meningitis), *Candida albicans* (0.6% of neonatal sepsis/meningitis), *Bacteroides fragilis* (0.3-5% of neonatal sepsis/meningitis), *Salmonella* (0.3% of neonatal sepsis/meningitis), *Prevotella disiens* (0-5% of neonatal sepsis/meningitis), *Peptostreptococcus magnus* (0-5% of neonatal sepsis/meningitis), *Clostridium perfringens*, *Neisseria gonorrhoeae*, *Haemophilus aprophilus,* coxsackievirus B (myocarditis, hepatitis), *simplexvirus* (1-1.5% of pregnancies, 85% of neonatal herpes; risk 3-60% if present at delivery; increased risk if maternal primary infection, premature rupture of membranes, delayed delivery; subsp 1 and 2 both of equal severity, subsp 2 most common; maternal genital source in ≈ 75%, also maternal non-genital and non-maternal (indirect transmission from another infant in nursery, ≈ 10% of symptomless hospital staff excrete *simplexvirus* in saliva); mortality 61% in disseminated disease; 50% of survivors have severe sequelae; 43% skin, eye and mouth (complete recovery with rapid antiviral treatment, ≤ 75% untreated advance to CNS or disseminated disease), 34% CNS (≥ 50% mortality), 23% disseminated (70% mortality)), *human cytomegalovirus* (10% localised to salivary glands, 1-2% disseminated; 88% kidney, 79% liver, 69% lung, 57% pancreas; 60% of neonates breastfed by mothers excreting *human cytomegalovirus* in breast milk, 55% of neonates born to mothers excreting *human cytomegalovirus* in cervical secretions; no neonates infected by mothers excreting only in urine or saliva; asymptomatic viruria in 20% of infants of seropositive mothers, 30% of third semester viruric mothers, 57% of postpartum and third semester viruric mothers, viruria delayed for 6 w; pneumonia in premature or (uncommonly) full term infants—'gray pallor', hepatosplenomegaly, respiratory distress, viruria), echovirus 6, 11, 14, 19 (hepatitis), HIV (transmission rate from 15% in Europe to 50% in Africa), *Streptococcus pneumoniae*, *Hafnia alvei, Streptococcus pyogenes*

Diagnosis: Gram stain and culture of gastric aspirate, throat swab, eye swab; Gram stain, immunofluorescence or PCR, electron microscopy, bacterial and viral culture of skin lesions swabs; Gram stain, culture and latex agglutination of CSF; blood cultures; viral culture of saliva, gastric washings and urine; serology; ELISA; C-reactive protein and interleukin levels (combined sensitivity 58-96%)

***Listeria monocytogenes*:** septicemia, often with meningitis; white cell count 13,600/μL, 36% neutrophils, 4% bands, 55% lymphocytes, 3% monocytes, 0.4% eosinophils

***Human cytomegalovirus*:** culture negative specimens at birth but positive specimens at ≥ 4 w; IgG antibody

HIV: ELISA, Western blot (immunoblot)

Enteroviruses, *Simplexvirus*: virus isolation; PCR; 1/3 herpes cases with CNS disease, 23% disseminated

Treatment:

***Streptococcus*, *Peptostreptococcus*, *Corynebacterium* and *Clostridium*:** benzylpenicillin

Other Anaerobes: metronidazole

Coliforms: gentamicin, chloramphenicol

***Neisseria gonorrhoeae*:** benzylpenicillin 75,000-100,000 U/kg i.v. daily in 4 divided doses for 7-10 d

Penicillinase-producing: cefotaxime or gentamicin

***Staphylococcus aureus*:** cloxacillin

***Listeria monocytogenes*:** benzylpenicillin 500,000-1 MU daily i.v. for 2 w or ampicillin + gentamicin 5 mg/kg daily in divided doses for 14-21 d

Haemophilus influenzae:

β-lactamase Negative: ampicillin for 7 d

β-lactamase Positive: ceftriaxone or cefotaxime

***Simplexvirus*:** aciclovir 20 mg/kg i.v. every 8 h (preterm: 12 h) for at least 14 d (localised) or 21 d (disseminated) (adjust dose for renal function)

Prevention and Control:

Neonatal *simplexvirus*: good hygiene (soap and water inactivate *simplexvirus*); monitor patients with history of herpes genitalis or with a history of sexual contact with a *simplexvirus*-infected partner; culture cervix and any recurrence site at 32, 34 and 36 w and once a week subsequently and tell patient to report any prodrome to her physician; patients with active disease (lesion visible) or positive culture should have elective caesarean section before membrane rupture

***Streptococcus agalactiae*:** screening of pregnant women at 35-37 w gestation by culture of combined vaginal and rectal swabs or by PCR at time of labour, and administration of benzylpenicillin (1.2 g i.v. stat, then 600 mg i.v. 4 hourly until delivery), or clindamycin (450 mg i.v. 8 hourly until delivery) or lincomycin (600 mg i.v. 8 hourly until delivery) if penicillin hypersensitive, to carriers

HIV: zidovudine 2 mg/kg i.v. over 1 h to mother 4 h before caesarean section before membrane rupture (reduces transmission rate to 2%), then 1 mg/kg per hour i.v. until the umbilical cord is clamped; zidovudine 2 mg/kg orally 6 hourly or 4 mg/kg orally 12 hourly to baby after umbilical cord is clamped or within 6-8 h of delivery and continued for first 6 w

POSTNATAL GENERALISED INFECTIONS

Agents: late-developing or postpartum infection with any of the agents listed in **PRENATAL GENERALISED DISEASE** and **PERINATAL GENERALISED DISEASE**

POSTNATAL GASTROENTERITIS

Agent: echovirus

Diagnosis: serology; viral culture of feces

Treatment: rehydration

ABORTIONAL AND PUERPERAL INFECTION: 0.01% of new episodes of illness in UK

Agents: 75% *Peptostreptococcus* + *Bacteroides*, 5% *Bacteroides* alone, 15% *Mycoplasma hominis*; *Streptococcus pyogenes* (produces peritonitis and septicemia), coliforms (post-abortion; produce endotoxic shock), *Staphylococcus aureus* (produces pneumonia and septicemia; derived from hospitalisation, i.v. therapy), *Enterococcus faecalis*, *Pseudomonas* (gives endotoxic shock), *Clostridium* (post-abortion, uterine tumours, complicated deliveries requiring mechanical intervention; endometritis, gross hemolysis, shock, uterine gas gangrene with fulminant septicemia), *Haemophilus influenzae*, *Aeromonas* (incomplete abortion); anaerobes isolated from blood cultures in 76% of cases of septic abortion complicated by bacteremia

Diagnosis: Gram stain and culture of swabs, pus; when possible, use culdocentesis to obtain specimens from the female genital tract after decontaminating the vagina with povidone iodine; double catheter and bronchial brush or sterile swab may be used for specimens from the uterine cavity; blood cultures

Treatment:

Patient Febrile but Not Clinically Ill: amoxycillin-clavulanate 500/125 mg orally 8 hourly for 3 d

Fever > 48 h: as above + erythromycin 500 mg orally 8 hourly or clindamycin 300 mg orally 8 hourly until fever resolves

Severely Ill: see **SEPTICEMIA**

***Clostridium*:** penicillin 20-30 MU/d i.v., chloramphenicol, metronidazole, clindamycin, cefoxitin

AMNIONITIS

Agents: *Streptococcus agalactiae*, *Listeria monocytogenes*, *Haemophilus influenzae*, *Capnocytophaga*, *Gardnerella vaginalis*, *Streptobacillus moniliformis,* anaerobes

Diagnosis: culture of amniotic fluid

Treatment: ampicillin + metronidazole

CHORIOAMNIONITIS

Agents: 22% anaerobes, 17% *Streptococcus agalactiae*, 22% other β-haemolytic streptococci, 17% coliforms, 6% *Mycoplasma hominis*, 6% *Ureaplasma urealyticum*, 6% *Haemophilus influenzae*, 6% *Gardnerella vaginalis*, *Corynebacterium striatum* (rare), *Capnocytophaga* (rare)

Diagnosis: culture of membrane

Treatment:

***Mycoplasma, Ureaplasma*:** erythromycin

Others: amoxycillin-clavulanate, cefotaxime

ENDOMETRITIS: early (≤ 48 h) postpartum following caesarean section, late (48 h - 6 w) postpartum usually following vaginal delivery

Agents: *Gardnerella vaginalis*, *Peptococcus*, *Staphylococcus epidermidis, Streptococcus agalactiae, Mycoplasma hominis* (34% of post-caesarean sections), *Ureaplasma urealyticum*, *Chlamydia trachomatis*, *Streptococcus pneumoniae;* also non-postpartum due to *Bacteroides*, *Prevotella bivia, Haemophilus influenzae* and *Actinomyces israelii* (IUD-related), *Vibrio vulnificus* (in a woman engaging in sex in sea water)

Diagnosis: protected, triple lumen transcervical culture (double catheter and bronchial brush or sterile swab specimens are not suitable because of contamination with vaginal flora)
Treatment: piperacillin, cefoxitin

Chapter 6

Infections of the Central Nervous System

MENINGITIS: in children with bacteremia, 15% of all children and 5% of children < 1 y not receiving antibiotic at time develop meningitis after lumbar puncture; poor prognosis if coma, delay in starting therapy, CSF glucose < 10 mg/dL, protein > 300 mg/dL, bacteremia (found in nearly all fatal cases), coexisting illness; overall fatality rate 4-20%; total rate of sequelae in survivors 4%; complications: 32% headache, 31% difficulty in concentrating, 24% loss of memory, 23% hearing impairment, 21% dizziness, 18% visual disturbances, 5% convulsions, 20% no complaint

Agents (Bacterial): 45-46% *Haemophilus influenzae* type b (case-fatality rate 3-7%), 14-27% *Neisseria meningitidis* (47% of meningococcal infections; case-fatality rate 0.4-14%), 13-19% *Streptococcus pneumoniae* (case rates 1-2/100,000; case-fatality rate 19-30%; 3% in < 5 y, 31-60% in > 60 y; neurologic sequelae widespread in survivors), 3-6% *Streptococcus agalactiae* (case-fatality rate 12-24%), 2-3% *Listeria monocytogenes* (case-fatality rate 22-30%), anthrax

Diagnosis: sudden onset of fever, headache, nausea, vomiting, signs of meningeal irritation, delirium, coma; blood cultures within 30 minutes of initial assessment; lumbar puncture if patient has none of anticoagulant therapy, bleeding diasthesis, signs of localised spinal sepsis, history of CNS disease, focal neurological signs, papilledema, new onset seizure, abnormal level of consciousness (adults) or rapidly deteriorating consciousness or obtundation (children) or immunosuppression, or if CT scan shows lumbar puncture not contraindicated; microscopy, Gram stain (positive in 25% of bacterial with $\leq 10^3$ cfu/mL and 97% with $\geq 10^5$, 70% positive in *Haemophilus influenzae*), chemistry and culture of CSF; acridine orange stain detects bacteria causing meningitis at $\geq 10^4$ cfu/mL in 10 minutes; CSF lactate (elevated in bacterial meningitis; enzymatic method or gas liquid chromatography < 1 h; distinguishes bacterial from viral meningitis; false positive and negative reactions occur); C-reactive protein determination on CSF (97% positive in bacterial meningitis, 50% in intracranial hemorrhage, 44% in Kawasaki syndrome, 30% in malignancies, 20% in neurological symptoms without infection, 6% in fever without bacterial meningitis and in increased intracranial pressure secondary to pseudotumour cerebri or hydrocephalus, negative in viral meningitis); coagulation (common organisms causing meningitis detected in CSF in < 5 min; may require treating specimen to eliminate nonspecific agglutination; *Haemophilus influenzae* type b sensitivity 77-100%, specificity 97-100%; *Streptococcus pneumoniae* sensitivity 71%, specificity 96%; *Neisseria meningitidis*; *Streptococcus agalactiae*); latex agglutination (false positives and negatives); counterimmunoelectrophoresis (difficult, less sensitive, more time-consuming) of CSF (results in < 1 h; *Haemophilus influenzae* type b sensitivity 67%, specificity 67%; *Neisseria meningitidis* A, B, C and W135 sensitivity 50%, specificity 50%; *Streptococcus pneumoniae*; *Streptococcus agalactiae*), serum (*Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*) and urine (*Haemophilus influenzae*, *Streptococcus pneumoniae*); gas liquid chromatography (detects anaerobes and selected aerobes in CSF in < 1 h; difficult sample preparation; research tool); limulus lysate (research tool; endotoxin determination detects Gram negative bacteria in CSF in < 2 h; 97% sensitivity and 99% specificity for *Haemophilus/Neisseria*); ELISA (higher sensitivity than counterimmunoelectrophoresis but more time-consuming and results not available same day); if tests normal, look for other explanation of signs and symptoms; if clearly suggestive of viral etiology, no specific therapy; if unclear, observe patient and repeat lumbar puncture if condition worsens or in 8-24 h; if clearly suggestive of 'chronic meningitis', perform appropriate smears and cultures and start immediate therapy or await results and further testing depending on clinical situation; if clearly suggestive of suppurative bacterial etiology, start appropriate antimicrobial therapy as indicated by Gram stain and/or other tests immediately or treat empirically as below

Bacterial Meningitis: CSF white cell count > 1000/µL (if > 50,000/µL, consider ruptured brain abscess), > 60% polymorphs, red blood cells absent, glucose < 45 mg/dL ($\leq$ 1 mmol/L; < 40-66% of blood glucose; normal in 40-50%), protein > 80 mg/dL, Gram stain positive in 80% (60% in partially treated), culture positive in 90% (66% in partially treated); peripheral blood leucocyte count > $16x10^9$/L; broad range bacterial PCR (sensitivity 100%, specificity 98%, positive predictive value 94%, negative predictive value 100%)

Viral Meningitis: CSF white cell count < 1000/μL in 83% (rarely > 2800/μL), polymorphs increased in 10%, lymphocytes increased, red blood cells variable, glucose normal, protein normal or slightly increased, Gram stain and bacterial culture negative

Fungal Meningitis: CSF white cell count < 5000/μL, lymphocytes increased, red blood cells absent, glucose normal or slightly decreased, protein > 60 mg/dL, Gram stain and bacterial culture negative

Tuberculous Meningitis: CSF white cell count < 1000/μL, polymorphs increased, red blood cells absent, glucose < 45 mg/dL, acid-fast stain positive in 80% if 10 mL of CSF centrifuged and sediment examined for 30-90 minutes, acid-fast bacilli culture positive in 85%

Carcinomatous Meningitis: CSF white cell count 0-500/μL, 0-95% polymorphs, red blood cells variable, glucose decreased or normal, protein usually increased, Gram stain and bacterial culture negative

Brain Abscess: CSF white cell count 10-500/μL, red blood cells variable, glucose decreased in 25%, protein increased in 75%, Gram stain positive in < 10%, culture positive in 16%

Endocarditis: CSF white cell count < 50/μL, polymorphs increased in 28%, lymphocytes increased in 25%, red blood cells occasionally raised, glucose normal or decreased, protein normal or increased, bacterial culture positive in 16%

Traumatic Tap: leucocytes:erythrocytes ≈ 1:500

Note that contaminating bacteria may be obtained from slides on which smears are made, tubes in which CSF is collected, needles and syringes in which CSF taken, stains used for staining smear

Treatment: see categories below; if bacterial meningitis is suspected, immediately administer benzylpenicillin (< 1 y: 300 mg; 1-9 y: 600 mg; ≥ 10 y: 1200 mg) or ceftriaxone 50 mg/kg to 2 g i.v. if penicillin hypersensitive or likely delay of > 6 h in further therapy and transfer to hospital; in hospital, dexamethasone 0.15 mg/kg to 10 mg i.v. +

Community Acquired: ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 7-10 d or cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7-10 d (+ benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 7-10 d or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7-10 d if *Listeria monocytogenes* suspected or immunosuppressed)

Gram Positive Cocci Seen, Pneumococcal Antigen Assay Positive, Neutrophils But No Organisms Seen: add vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

Immediate Penicillin or Cepahlosporin Hypersensitivity: vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly by slow infusion (monitor blood levels and adjust dose accordingly) + ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly or moxifloxacin 10 mg/kg to 400 mg i.v. daily

Neisseria meningitidis: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 3-5 d, then ceftriaxone 250 mg (child 125 mg) i.m. as single dose or ciprofloxacin 500 mg orally as single dose (≥ 12 y) or rifampicin 10 mg/kg to 600 mg (< 1 mo: 5 mg/kg) orally 12 hourly for 2 d and/or immunisation; activated protein C; steroids

Penicillin Hypersensitive (Not Immediate): ceftriaxone 100 mg/kg to 4 g i.v. daily for 3-5 d or 50 mg/kg to 2 g i.v. 12 hourly for 3-5 d or cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 3-5 d

Immediate Penicillin or Cephalosporin Hypersensitive: ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly for 3-5 d

Streptococcus pneumoniae:

Penicillin MIC < 0.125 mg/L: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 10-14 d

Penicillin MIC ≥ 0.125 mg/L: vancomycin 15 mg/kg to 500 mg i.v. 6 hourly + cefotaxime 50 mg/kg to 2 g i.v. 6 hourly or ceftriaxone 50 mg/kg to 2 g i.v. 12 hourly

***Haemophilus influenzae* type b:**

Penicillin Susceptible: benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly for 7 d or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7 d

Penicillin Resistant: ceftriaxone 100 mg/kg to 4 g i.v. daily for 7 d or 50 mg/kg to 2 g i.v. 12 hourly for 7 d or cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7 d

Immediate Penicillin or Cephalosporin Hypersensitive: chloramphenicol 20-25 mg/kg to a g i.v. 6 hourly for 7 d or ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly for 7 d

Listeria monocytogenes: benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

Penicillin Hypersensitive: cotrimoxazole 4/20 mg/kg to 160/800 mg i.v. 6 hourly

Anthrax: ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly + benzylpenicillin or amoxy/ampicillin or chloramphenicol

Health Care-Associated: vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly + ceftazidime 50 mg/kg to 2 g i.v. 8 hourly or meropenem 40 mg/kg to 2 g i.v. 8 hourly

Prophylaxis

Neisseria meningitidis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

***Haemophilus influenzae* type b:** given to index case before discharge, to all household contacts of another child who is incompletely immunised against *Haemophilus influenzae* type b and to all household contacts of index case < 2 y; rifampicin 20 mg/kg to maximum 600 mg (child < 1 mo: 10 mg/kg) orally daily for 4 d (not pregnant; give ceftriaxone 1g in lignocaine hydrochloride 1% i.m. as single dose); vaccine to index case under 2 y even if previous immunisation and to unvaccinated contacts < 5 y

Streptococcus pneumoniae: pneumococcal polysaccharide vaccine recommended to adults ≥ 65 y, individuals > 2 y with chronic illness, anatomic or functional asplenia, immunocompromise (disease, chemotherapy, steroids), HIV infection, environment or settings with increased risk, or cochlear implants; pain, swelling and redness at injection site in 30-50%, fever and muscle aches in < 1%, rare severe reactions; revaccination after 5 y for ≥ 2 y with functional or anatomic asplenia, immunsuppression, malignancy, transplant, chronic renal failure, nephritic syndrome, HIV infection, chronic systemic steroids, or < 65 y at time of first vaccination; pneumococcal conjugate vaccine recommended for routine vaccination of children < 24 mo and 24-59 mo with high risk medical conditions; pain, swelling and redness at injection site in 10-20%; reduces invasive disease due to serotypes in the vaccine by 97% and to those not in the vaccine by 89%

NEONATAL MENINGITIS: incidence 28/100 000 live births; case-fatality rate 26-27%; high morbidity; ventriculitis

Agents: 50-60% Gram negative bacilli (11-47% *Escherichia coli* (early and late; increased risk in galactosemia), 5% *Pseudomonas aeruginosa*, 0-16% *Klebsiella pneumoniae* (mainly late), 0-7% *Serratia*, 0-3% *Haemophilus influenzae* (50% of cases associated with maternal complication; 83% in premature infants; 33% mortality); *Proteus*, *Salmonella*, *Citrobacter diversus* (brain abscess common), *Enterobacter sakazaki,* other coliforms, *Flavobacterium meningosepticum* (virulent; always nosocomial), *Campylobacter fetus* subsp *fetus*), 24-34% *Streptococcus agalactiae* (mainly early; case-fatality rate 24%), 2-10% *Listeria monocytogenes* (early and late; case-fatality rate 30%), 0-7% *Streptococcus pneumoniae* (early), 0-5% *Staphylococcus aureus* (late), 0-5% *Enterococcus* (early), group C *Streptococcus*, *Streptococcus mitis, Bacillus* (very rare), *Neisseria gonorrhoeae*, *Sphingobacterium mizutaii* (prematures), *Alcaligenes xylosoxidans, Aeromonas*

Diagnosis: Gram stain and acridine orange stain of cytocentrifuged specimen of CSF; micro and culture of CSF; latex agglutination of concentrated urine, CSF and serum; counterimmunoelectrophoresis of CSF; ELISA

***Haemophilus influenzae*:** CSF protein 486 mg/dL, glucose 39 mg/dL, leucocytes 11,500/μL, 90% polymorphonuclears; latex agglutination on CSF (sensitivity 77-100%, specificity 97-100%); radioimmunoassay (sensitivity 95%)

***Listeria monocytogenes*:** opening pressure > 200 mm H_2O, protein 100-200 mg/dL, glucose 30-100 mg/dL (≥ 50% serum glucose), leucocytes 100-4000/μL, 75-100% polymorphs, Gram stain positive in 50%

***Streptococcus agalactiae*:** latex agglutination on concentrated urine (sensitivity 93%), CSF (sensitivity 80%), serum (sensitivity 27%); radioimmunoassay

Treatment: dexamethasone or oxindanac +:

Enteric Gram Negative Bacilli or Organism Nor Known: cefotaxime 200 mg/kg daily in 4 equal divided doses or ceftriaxone 100 mg/kg daily in 2 equal divided doses + aminoglycoside for 21 d

***Flavobacterium meningosepticum*:** rifampicin

Streptococcus pneumoniae:

Penicillin MIC ≤ 0.125 mg/L: benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 10 d

Penicillin MIC > 0.125 mg/L: ceftriaxone or cefotaxime + vancomycin or rifampcin

***Streptococcus agalactiae*:** benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly for 14-21 d

***Listeria monocytogenes*:** cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

***Pseudomonas aeruginosa*:** azlocillin 225 mg/kg i.v. daily in 3 divided doses or ceftazidime 100-200 mg/kg i.v. daily in divided doses + amikacin 5 mg/kg i.v. 8 hourly during first week; ticarcillin 200-300 mg/kg i.v. daily in divided doses every 4-6 h + tobramycin 1.5-2.5 mg/kg 8 hourly

***Neisseria gonorrhoeae*:** benzylpenicillin 100 000 U/kg i.v. daily in 4 divided doses for at least 10 d

POST-NEONATAL PURULENT MENINGITIS: commonly related to upper respiratory infection with invasion of subarachnoid space by organisms arising from nasopharynx or by septicemic spread from lungs; also to urinary tract infection in the aged; ≈ 9 cases/100,000 person-years; case-fatality rate 14%

Agents: 40-46% (40-60% in aged 1 mo - 15 y, 1-3% in > 15 y) *Haemophilus influenzae* (usually type b; cosmopolitan; 1.2/100,000 total, 59/100,000 age 6-8 mo; case-fatality rate 4-7%; exclude CSF leak in adult; 29% associated with acute otitis media; more common isolate in antibody-mediated deficiency and asplenism, less frequent isolate in granulocyte disorders; also associated with spinal cord trauma; 8% of bacteremic and 8% of nonbacteremic invasive *Haemophilus influenzae* infections in older children and adults; ≈ 40 notified cases/y in Australia; neurologic sequalae (hearing impairment, mental retardation, seizure disorder, developmental delay, paralysis) in 15-30%), 27-29% (25-40% in aged 1 mo - 15 y, 10-35% in > 15 y) *Neisseria meningitidis* (epidemic cerebrospinal meningitis, epidemic meningitis, diplococcal meningitis, meningitis Neisseria, meningococcic meningitis; usually types A, B, C; particularly prevalent in Subsaharan Africa, Middle East and upland parts of Indian subcontinent; 0.7/100,000 total, 13/100,000 age 3-8 mo; case-fatality rate 0.4-14%; ≈ 600 notified cases/y in Australia (≈ 40% in New South Wales); usually arising as a result of hematogenous spread from asymptomatic colonisation of nasopharynx or from meningococcal nasopharyngitis, with an intervening phase of meningococcal septicemia or of asymptomatic meningococcal bacteremia; 14% associated with acute otitis media; epidemics and may be acute (sometimes fulminant) or chronic; spread may affect optic and other nerves; less frequent isolate in granulocyte disorders and antibody-mediated deficiency, infrequent isolate in asplenism; transmission respiratory; incubation period 2-10 d), 11-13% (10-20% in aged 1 mo - 15 y, 30-50% in > 15 y) *Streptococcus pneumoniae* (0.3/100,000 total, 8/100,000 age 3-5 mo; case-fatality rate 19-28%; sequelae common in survivors: 54% neurological, 42% neuropsychological, 25% otological, 16% various degrees of cerebral and cerebellar atrophy; 33% associated with acute otitis media; also from pulmonary focus, sinusitis; common isolate in granulocyte disorders, antibody-mediated deficiency and asplenism; also associated with cranial defect from previous head and spinal cord trauma; more common in infants, elderly, alcoholics), 3% *Streptococcus agalactiae* (0.1/100,000 total, 42/100,000 age < 1 mo; case-fatality rate 12-24%), 1% other streptococci (case-fatality rate 44%; 22% associated with brain abscess; also associated with ventriculoatrial and other shunts; *Streptococcus pyogenes* and *Enterococcus faecalis* infrequent isolates in granulocyte disorders and AIDS; *Streptococcus pyogenes* less common isolate in antibody-mediated deficiency, infrequent isolate in asplenism; community acquired; otitis media, pharyngitis or sinusitis usually present; *Streptococcus suis* in pig workers; *Streptococcus canis*), 1-9% *Staphylococcus aureus* (case-fatality rate 27% overall, 56% in hematogenous, 18% in postoperative; 18% associated with acute otitis media, 18% associated with pneumonia; common isolate in granulocyte disorders, less common isolate in antibody-mediated deficiency; also associated with surgery, ventriculoatrial and other shunts, nosocomial infections, foreign body, parameningeal or brain abscess), 1% mixed bacteria (children, adults with contiguous infection or tumour or fistulous communication with CNS); *Listeria monocytogenes* (1-2% in age 1 mo - 15 y, 5% in > 15 y; in lymphoproliferative malignancy, lung carcinoma, neonates, immunosuppressed, elderly, others; case-fatality rate 22-30%), enteric Gram negative bacilli (1-2% in age 1 mo - 15 y, 1-10% in > 15 y; *Escherichia coli* (usually K1; sepsis—respiratory tract infection or pneumonia; immunocompromised and immunosuppressed; common isolate in granulocyte disorders, infrequent isolate in asplenism; also associated with head trauma, neurological procedure and nosocomial infections), *Klebsiellla* (less frequent isolate in granulocyte disorders), *Enterobacter* (less frequent isolate in granulocyte disorders), *Proteus* (infrequent isolate in granulocyte disorders), *Serratia* (nosocomial; mainly neonates and infants), *Salmonella*), *Pseudomonas aeruginosa* (10% of cases in cancer patients; common isolate in granulocyte disorders, less common isolate in antibody-mediated deficiency; also associated with surgery and nosocomial infections), *Burkholderia cepacia, Stenotrophomonas maltophilia, Neisseria gonorrhoeae*, *Neisseria lactamica* (following skull trauma), *Neisseria mucosa* (female infants and children with predisposing

conditions), *Neisseria subflava, Neisseria flavescens, Moraxella catarrhalis*, *Moraxella lacunata, Moraxella osloensis, Bacteroides* (associated with surgery), *Dialister pneumosintes* (chronic), *Francisella tularensis* (rare), *Campylobacter fetus* subsp *fetus* (rare), *Campylobacter jejuni* (rare), *Aeromonas hydrophila* (infrequent isolate in granulocyte disorders, others), *Aeromonas sobria* (rare isolates in chronic alcoholic liver disease), *Flavobacterium meningosepticum* (in immunocompromised), *Acinetobacter* (nosocomial; mainly associated with indwelling ventriculostomy tubes or CSF fistulae in patients receiving antimicrobials), *Yersinia pestis* (rare complication of bubonic plague), *Pasteurella multocida* (rare; animal contact; case-fatality rate 30%), *Bacillus* (*Bacillus anthracis*: hemorrhagic meningitis (anthrax meningitis, meningeal anthrax) as complication in about 5% of cases of anthrax (39% inhalational, 29% cutaneous, 17% gastrointestinal, 16% unknown); and cases with no primary focus (up to 59% in some outbreaks in India), other species (especially *Bacillus cereus*) in immunocompromised, infrequent isolate in granulocyte disorders), *Clostridium* (infrequent isolate in granulocyte disorders; also associated with head and spinal cord trauma), diphtheroids (associated with ventriculoatrial and other shunts), *Corynebacterium bovis* (rare), *Nocardia asteroides* (common in impaired cell-mediated immunity; case-fatality rate 57%), *Kingella kingae* (sickle cell anemia), *Bergeyella zoohelcum, Capnocytophaga canimorsus, Bordetella bronchiseptica* (posttraumatic), *Vibrio cincinnatii, Plesiomonas shigelloides, Haemophilus parainfluenzae, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Aerococcus viridans* (rare), *Fusobacterium necrophorum* (uncommon), *Candida* (infrequent isolate in granulocyte disorders and asplenism; also nosocomial and in AIDS), *Coccidioides immitis* (25% of AIDS patients in endemic areas), *Histoplasma capsulatum* (in AIDS; ≈ 60% fatality rate), *Ajellomyces dermatitidis* (AIDS), *Aspergillus* (rare in AIDS), *Plasmodium malariae* (infrequent isolate in asplenism), *Plasmodium falciparum* (in therapy for nutritional deficiency), *Trichomonas* (associated with surgery), almost any other pathogen

Diagnosis: micro (≥ 1000 polymorphs/μL), protein (100-1000 mg/dL), glucose (< 1/3 of blood), culture, latex agglutination and C-reactive protein on CSF; Gram stain and acridine orange stain on cytocentrifuged CSF; counterimmunoelectrophoresis on serum and urine; ELISA on urine; latex agglutination on serum; increased lactic acid in CSF

***Neisseria meningitidis*:** hemorrhagic skin lesions; protein 770 mg/dL, glucose 6 mg/dL, leucocytes 20,700-212,000/μL, 98% neutrophils, multiple extracellular and intracellular Gram negative diplococci; direct immunofluorescence and ELISA of CSF; latex agglutination of CSF (sensitivity 33%, specificity 100%)

***Streptococcus pneumoniae*:** slight enlargement of lateral ventricles on air encephalogram; mild communicating hydrocephalus on computerised axial tomography; CSF 9000 neutrophils/μL, 100 lymphocytes/μL; direct immunofluorescence of CSF; latex agglutination of CSF (sensitivity 71-100%, specificity 96%); radioimmunoassay; white cell count 17,400/μL, 87% neutrophils, 2% bands

***Haemophilus influenzae*:** septic arthritis, cellulitis of face or upper extremity; can be fulminant but commonly mild illness followed by significant deterioration; protein 486 mg/dL, glucose 39 mg/dL, leucocytes 11,500/μL, 90% polymorphonuclears; ELISA on CSF; latex agglutination on CSF (sensitivity 77-100%, specificity 97-100%), radioimmunoassay (sensitivity 75%)

***Listeria monocytogenes*:** opening pressure > 200 mm H_2O, protein 100-200 mg/dL, glucose 30-100 mg/dL (≥ 50% serum glucose; depressed in 60%), leucocytes 100-4000/μL, 75-100% polymorphs changing to 98% mononuclears; Gram stain positive in 50%

***Staphylococcus aureus*:** fever in 75-90%, altered mental status in 38-55%; CSF protein > 80 mg/dL in 83-86%, CSF glucose < 50% of serum level in 57-67%, CSF white cell count > 5/μL in 83-88%, > 1000/μL in 34%, > 66% neutrophils in 80-100%; Gram stain positive in 40-62%; blood culture positive in 60-86%

***Nocardia asteroides*:** subacute to chronic presentation; 68% fever, 66% stiff neck, 55% headache; neutrophil pleocytosis; 83% > 500 leucocytes/μL, 66% < 40 mg glucose/dL, 61% > 100 mg/dL protein; 43% associated brain abscess; histology and culture of tissue

Anthrax: fever, malaise, meningeal signs, hyperreflexia, delirium, stupor, coma; hemorrhagic meningitis, multifocal subarachnoid and intraparenchymal hemorrhages, vasculitis, cerebral edema; 94% case-fatality rate (75% within 24 h of presentation); Gram stain, India ink stain and culture of CSF sediment; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test

Bacillus cereus: diarrhoea, fever, altered mental status; Gram stain and culture of CSF

***Candida*:** glucose decreased and protein increased in 60% of cases; leucocytes 6000/μL (lymphocytes and neutrophils); organisms in Gram stain in 40%; culture of biopsy

Coccidioides immitis: EIA of CSF using combination of antigens (sensitivity 100%, specificity 96%), RIA of CSF (sensitivity 100%), overnight binding complement fixation test on CSF (sensitivity 95%)

Histoplasma capsulatum: RIA or EIA for histoplasma polysaccharide antigen in body fluids (sensitivity 90-97%), culture of bone marrow, lymph nodes, ulcers (positive in 90%), CSF (often negative)

Ajellomyces dermatitidis: EIA using purified antigen A (false positives in some cases of histoplasmosis and sporotrichosis)

Aspergillus: stroke or intracranial hemorrhage in immunosuppressed HIV-positive patient with single or multiple contrast-enhancing lesions; CSF nonspecifically abnormal, culture usually negative; serology insensitive

Treatment: dexamethasone 3 mg/kg i.v. initially followed by 1 mg/kg 6 hourly over period of 48 h or oxindanac +:

Neisseria meningitidis: benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 5-7 d; i.v. heparin + i.v. hydrocortisone if any evidence of Waterhouse-Friderichsen syndrome

Neisseria gonorrhoeae: ceftriaxone 1-2 g i.v. every 12 h

Penicillin Susceptible Streptococci (MIC < 0.125 mg/L): benzylpenicillin + aminoglycoside if warranted

Penicillin Hypersensitive Patient with *Neisseria*, Any Patient With Relatively Resistant (MIC 0.125- ≤ 1 mg/L) *Streptococcus pneumoniae*: cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 5-7 d or ceftriaxone 200 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 5-7 d

Penicillin Resistant (MIC > 1 mg/L) or Cefotaxime Resistant *Streptococcus pneumoniae*: ceftriaxone + vancomycin 2 g every 12 h or rifampicin; seek specialist advice

***Haemophilus influenzae*:** cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7-10 d, ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 7-10 d, (amoxy)ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7-10 d (if susceptible)

Staphylococci: oxacillin 200 mg/kg/d to 12-16 g/d 4-6 hourly, vancomycin 60 mg/kg/d up to 2 g/d 6-12 hourly

***Francisella tularensis*, *Yersinia pestis*:** streptomycin

***Campylobacter*:** chloramphenicol

***Flavobacterium meningosepticum*:** sulphadiazine + rifampicin

***Pseudomonas aeruginosa*:** azlocillin 3 g i.v. 4 hourly (child: 225 mg/kg i.v. daily in 3 divided doses) or ceftazidime 6-12 g (child: 100-200 mg/kg) i.v. daily in divided doses for 9-50 d + amikacin 5mg/kg i.v. 8 hourly during first week; ticarcillin 3 g i.v. 4 hourly (< 40 kg: 200-300 mg/kg i.v. daily in divided doses every 4-6 h) + tobramycin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly, meropenem

Burkholderia cepacia: imipenem

***Stenotrophomonas maltophilia*:** cotrimoxazole ± rifampicin

***Moraxella catarrhalis*:** amoxycillin-clavulanate

Salmonella typhi: chloramphenicol 100mg/kg daily i.v. in 4 equally divided doses, substituting oral treatment as soon as possible

Enteric Gram Negative Bacilli: cefotaxime 2g i.v. 4 hourly (child: 200 mg/kg daily in 4 equally divided doses) or ceftriaxone 2-4 g i.v. daily (child: 100 mg/kg daily in 2 equally divided doses) + aminoglycoside for 21 d

***Bacteroides*:** metronidazole

***Acinetobacter*:** imipenem, minocycline, ciprofloxacin, polymyxin, ampicillin-sulbactam, cefperazone-sulbactam

***Pasteurella multocida, Kingella kingae*:** penicillin, ampicillin, third generation cephalosporin, chloramphenicol

Listeria monocytogenes: cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or (amoxy)ampicillin 50 mg/kg to 2 g i.v. 4 hourly

***Nocardia asteroides*:** sulphonamides, cotrimoxazole, minocycline 200 mg bid, amikacin for at least 6 mo; cefotaxime 2g i.v. 8 hourly + imipenem 500 mg i.v. 6 hourly in severely ill

Anthrax: ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly + penicillin or amoxy/ampicillin or chloramphenicol for 14-21 d then ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly or doxycycline 2 mg/kg to 100 mg orally 12 hourly (child: amoxycillin 15 mg/kg to 500 mg orally 8 hourly) for total 60 d

Bacillus cereus: vancomycin + carbapenem

Fungal: amphotericin B ± flucytosine

***Plasmodium*:** chloroquine

Others or Unknown: chloramphenicol 1 g i.v. 6 hourly ± benzylpenicillin 1.2-2.4 g i.v. 4 hourly

Hospital Acquired: vancomycin 15 mg/kg to 500 mg i.v. 6 hourly + cefotaxime 50 mg/kg to 2 g i.v. 6 hourly or ceftriaxone 50 mg/kg to 2 g i.v. 12 hourly or meropenem 40 mg/kg to 2 g i.v. 8 hourly

Prophylaxis:

Meningococcal (Index Case After Treatment and Close Contacts): ceftriaxone 250 mg (child 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); single 0.5 mL s.c. dose (adults and children > 2 y) of vaccine for *Neisseria meningitidis* types A, C, Y and W135 recommended for patients with deficiency of terminal complement component, travellers and long-term residents who will be living in or travelling through such endemic and hyperendemic areas as rural communities in Brazil, Burkina Faso, Chad, Egypt, Ghana, Mali, Mongolia, Nepal, Nigeria, Sudan, Vietnam, health care workers going to Saudi Arabia and Gulf States, in conjunction with antimicrobial prophylaxis for intimate contacts; mass immunisation may be indicated if several cases appear over a period of several weeks or if attack rates exceed 0.66-1.25/100,000 of population

***Haemophilus influenzae* type b:** given to index case before discharge, and within 7 d to all household contacts of index case, including incompletely immunised children < 4y and any immunocmpromsed child; also adults and children at day care centres with 2 or more cases of invasive disease in 60 d period and with incompletely immunised children; rifampicin 20 mg/kg to maximum 600 mg (child < 1 mo: 10 mg/kg) orally daily for 4 d (not pregnant; give ceftriaxone 1 g in lignocaine hydrochloride 1% i.m. as single dose); vaccine to index case under 2 y even if previous immunisation and to unvaccinated contacts < 5 y; all children should be routinely vaccinated beginning at 2 mo (95-100% efficacy; swelling, redness and pain at injection site in 5-30%, fever and irritability uncommon, serious reactions rare; contraindicated if anaphylaxis to vaccine components or previous dose and serious illnesses)

***Streptococcus pneumoniae*:** 1 dose of a 23 valent pneumococcal vaccine is recommended for adults with cardiovascular disease and chronic pulmonary disease entailing increased morbidity from respiratory infection, alcoholism, cirrhosis of liver, CSF leaks, diabetes mellitus, Hodgkin's disease, immunosuppression (preferably administered 6 w before initiation of immunosuppressive therapy), multiple myeloma, post-renal transplant, postsplenectomy, skull fracture with recurrent pneumococcal meningitis, splenic dysfunction and otherwise healthy adults aged 66 or older, and in children aged 2 y or older with anatomic splenectomy or persistent asplenism associated with sickle cells, CSF leaks, immunosuppression, nephrotic syndrome or splenectomy (administer 2 w before operation if possible)

Asplenic and Postsplenectomy: pneumococcal, meningococcal, Hib and standard schedule immunisation (including annual influenza); antibiotic prophylaxis in asplenic children < 5 y, children < 5 y with sickle cell anemia, for at least 2 y following splenectomy and patients with severe underlying immunosuppression: amoxycillin 125 mg orally 12 hourly (< 2 y: 20 mg/kg orally daily) or phenoxymethylpenicillin 250 mg (< 2 y: 125 mg) orally 12 hourly or if penicillin hypersensitive roxithromycin 4 mg/kg to 150 mg orally daily or erythromycin 250 mg orally daily or erthryomycin ethyl succinate 400 mg orally daily

CSF Fistula: may result in recurrent meningitis

Agent: especially *Streptococcus pneumoniae*

Diagnosis: recurrent meningitis, history of trauma, congenital anomalies; unilateral, clear, watery rhinorrhoea; hearing loss, especially unilateral; protein electrophoresis or ring test on fluid (rhinorrhoeal or otic) suspected of being CSF; high resolution CT in axial and coronal plane; MRI; contrast cisternography with iopanidole or iohexal, intrathecal injections of fluorescein diluted in CSF and observation of pledgets placed in sphenoethmoid region, cribriform area, roof of nasal cavity and eustachian tube orifice

Treatment: head elevation at angle of 45°; spinal drain if necessary; surgical correction (extracranial approach preferred) if persistent rhinorrhoea (> 5-7 d), recurrent meningitis or spontaneous rhinorrhoea from anterior, middle or posterior fossa

Non-pyogenic (Lymphocytic, Aseptic) Meningitis

Agents: 70% of cases unclassified; 70-79% of documented cases enterovirus (transmission fecal and respiratory; incubation period 1 to several weeks; infrequent infections in impaired cell-mediated immunity and in antibody-mediated deficiency); 54% *human echovirus* (23% of *human echovirus* infections; attack rate 107/100,000; 38%

human echovirus 11, 26% *human echovirus 30*, 21% *human echovirus 7*, 6% *human echovirus 4*, 3% *human echovirus 1*, 3% *human echovirus 17*, 3% *human echovirus 25*), 22% *human coxsackievirus B3*, 22% *human coxsackievirus B4*, 1% *human coxsackievirus B5*, remainder *human coxsackievirus A1*, *A2*, *A4-A7*, *A9*, *A10*, *A12*, *A14*, *A16*, *A22*, *echo 9 virus*, *human coxsackievirus B1*, *B2*, *B6*, *human echovirus 2-7*, *11, 13-21, 24, 25, 30, 31, 33*, *human parechovirus 1*, *human parechovirus* 2, other enteroviruses), 6% influenza A, 4-10% *simplexvirus* (common in impaired cell-mediated immunity), 4% *measles virus*, 4% arboviruses, 2-15% *human adenovirus*, 1-4% *mumps virus* (0.7/1000 mumps cases symptomatic but CSF pleocytosis in ≥ 50%), *poliovirus* (in 28% of poliovirus cases; infrequent infections in antibody-mediated deficiency and cell-mediated immunity deficiency), *lymphocytic choriomeningitis virus* (probably worldwide but not in Australia; often spread from mice and probably pet hamsters; frequently in children), *mengo encephalomyocarditis virus*, *simplexvirus 3* (common in impaired cell-mediated immunity), hepatitis viruses, *Epstein-Barr virus* (Duncan's syndrome), Kawasaki syndrome, reoviruses, *vaccinia virus* (postvaccination; infrequent infections in impaired cell-mediated immunity), *rubella virus*, *parainfluenza 3*, many other viruses, *Nocardia asteroides* (common in impaired cell-mediated immunity), *Mycobacterium tuberculosis* (1% of tuberculosis cases; fatality rate 15-40%; less common infection in impaired cell-mediated immunity; also in therapy for nutritional deficiency), *Brucella* (< 5% of cases of systemic brucellosis; infrequent infections in impaired cell-mediated immunity; also in therapy for nutritional deficiency), *Listeria monocytogenes* (common in impaired cell-mediated immunity), *Leptospira*, *Treponema pallidum* subsp *pallidum* (uncommon), *Mycoplasma hominis* (rare), *Mycoplasma pneumoniae*, *Cryptococcus neoformans* (see **Cryptococcal Meningitis**), *Coccidioides immitis* (see **Coccidioidosis**; travel to San Joaquin Valley), *Histoplasma capsulatum* (see **Histoplasmosis**), *Aspergillus* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Mucor* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Absidia* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Rhizopus* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Drechslera* (associated with lymphoma), *Candida* (uncommon), *Pseudallescheria boydii* (uncommon), *Toxoplasma gondii* (in immunosuppressed, particularly Hodgkin's disease; infrequent infections in impaired cell-mediated immunity), *Strongyloides stercoralis* (associated with corticosteroid treatment; extremely infrequent infections in impaired cell-mediated immunity), *Taenia solium* (infrequent infections in impaired cell-mediated immunity), *Trichinella spiralis*, myiasis (extremely infrequent infections in impaired cell-mediated immunity), *Naegleria* (see **Amoebic Meningoencephalitis**); also cancer, sarcoidosis, Behcet's disease, Mollaret's meningitis, systemic lupus erythematosus, Sjögren's syndrome, reaction to ibuprofen and other NSAIDS, azathioprine, tolmentin, zimeldin, trimethoprim and other antibiotics, carbamazepine, allopurinol, i.v. immunoglobulins, OKT3 monoclonal antibodies

Diagnosis: fever, signs of meningeal irritation (eg., stiff neck), variable degree of drowsiness, confusion, stupor, rarely coma, ≥ 10 lymphocytes/μL in CSF, no neurologic abnormality of recent onset; human coxsackievirus A2, A7, A9, B1, B2, B4, B5, *human echovirus 3, 4, 6, 9, 11, 14, 17, 18, 25, 30, 33*, *human parechovirus 1* and *2* and *human enterovirus 71* produce exanthem; Gram stain, acridine orange stain and acid-fast stain, culture and serology of CSF; blood culture using DuPont Isolator or Bactec fungal medium; viral culture of serum in RD and BGM cells; viral culture of feces and throat swab; complement fixation test, hemagglutination inhibition, neutralisation

Viral: protein normal or increased, glucose normal, chloride normal, cell counts normal to 25-100 lymphocytes/μL, polymorphs early in illness

Arboviruses: paired sera

Enteroviral: protein 15-100 mg/dL, glucose 44-86 mg/dL, 17-912 leucocytes/μL; positive serology in 17%; virus isolation

***Simplexvirus*:** PCR on CSF

***Lymphocytic choriomeningitis virus*:** paired sera

***Mumps virus*:** age 5-14 y, males > females, with parotitis in spring, without parotitis in summer; up to 2000 leucocytes/μL, usually lymphocytes predominant, but may be polymorphs; protein normal or very mildly increased, glucose normal or mildly decreased; sequelae extremely rare; encephalitis ≈ 1:5000 cases; virus isolation

***Epstein-Barr virus*:** persevereation, impulsivity, complex-partial seizures, emotional lability, obsessive-compulsive behaviour; CSF PCR

Mycobacterium tuberculosis: most commonly, complication of primary lung lesions in very young children, but also in adults; ophthalmoplegia or facial paralysis; headache in 86%, abnormal mental state in 57%, fever in 55%, night sweats or rigours in 52%; **CSF**: protein ≥ 200 mg/dL in 70-80% of cases (36% 1000-1500 mg/dL), glucose ≤ 45 mg/dL in 70-85% (26% 2.3-2.6 mmol/L), ≥ 100 leucocytes/µL in 60-80% (26% 200-400/µL), increased lymphocytes ± increased neutrophils (29% 0-10%); serial **AFB** smears positive in 87%; latex agglutination (sensitivity 100%, specificity 99%); **ELISA**; adenosine deaminase activity; **PCR**

Brucella: acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; **ELISA (IgA, IgG, IgM)**, 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Leptospira: protein increased, cell count 300-2000/µL; neutrophilia becoming lymphocytosis

Treponema pallidum subsp pallidum: **VDRL** positive in 90% of cases; protein 50-150 mg/dL (IgG increased), glucose normal, lymphocytes 10-500/µL

Listeria monocytogenes: protein generally increased, glucose decreased in 60%, leucocytes few to several thousand, polymorphs 0-100%

Aspergillus: protein increased, glucose decreased, cells variable

Zygomycetes: CSF normal

Metastatic Carcinoma, Lymphoma, Meningeal Sarcoma: glucose reduced

Differential Diagnosis: partially treated pyogenic meningitis, brain abscess, parameningeal focus of infection, subdural hematoma, subarachnoid hemorrhage, brain tumour, multiple sclerosis, malignant hypertension, thrombotic thrombocytopenic purpura, systemic lupus erythematosus, temporal arteritis, carcinomatous meningitis

Treatment:

Simplexvirus: aciclovir 5 mg/kg i.v. 8 hourly as a 1 h infusion for 14 d or vidarabine 15 mg/kg daily as a 12-24 h infusion for 10 d + dexamethasone

Other Viral: non-specific (disoxaril in persistent enteroviral infections in agammaglobulinemic individuals; corticosteroids in *Epstein-Barr*)

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 12 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 12 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (12 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 12 mo) + prednisolone 60 mg (child: 1-3 mg/kg) daily for 1-2 w, gradually reducing over next 4-6 w

Nocardia: cotrimoxazole, sulphonamides, minocycline, amikacin, imipenem for at least 6 mo

Brucella: doxycycline 100 mg orally twice a day + rifampicin 600 mg orally 4 times a day or streptomycin 1 g i.m. 4 times a day for 45 d, ciprofloxacin 500 mg orally twice a day + rifampicin 600 mg orally twice a day for 30 d

Treponema pallidum subsp pallidum: penicillin

Leptospira: oxytetracycline

Listeria monocytogenes: cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

Fungal: amphotericin B 0.75 mg/kg i.v. daily ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 14 d; diagnostic and therapeutic resection possibly helpful

Toxoplasma gondii: pyrimethamine 100-200 mg loading dose, then 50-100 mg/d orally + folinic acid 10 mg/d orally + sulphadiazine 4-8 g/d in divided doses; pyrimethamine 100-200 mg loading dose, then 50-100 mg/d orally + folinic acid 10 mg/d orally + clindamycin 900-1200 mg i.v. every 6 h or 300-450 mg orally every 6 h; spiramycin

Taenia solium: mebendazole

Strongyloides stercoralis: thiabendazole, albendazole

Prophylaxis: immunisation against *Poliovirus*; experimental antiviral drugs

Cryptococcal Meningitis: ≈ 0.2 cases/100,000 person-years; occurs in impaired cell-mediated immunity (particularly associated with lymphomas) but also in others
Agent: *Cryptococcus neoformans, Cryptococcus gatii*
Diagnosis: intermittent headache of increasing frequency and severity, usually frontal, temporal or postorbital, may be accompanied by vomiting and vertigo, confusion, personality change, decreased memory, meningeal signs (nuchal rigidity, positive Kernig's and Brudzinski's signs) in 50% of cases, cranial nerve involvement (hearing loss, diplopia, ophthalmoplegia, facial nerve palsy) in 20%, increased cranial pressure hyperreflexia, pathologic reflexes, ataxia, convulsions, fever, progressive delirium and psychosis in 10%; CSF protein increased (50-200 mg/dL), glucose normal to slightly low, 25-500 leucocytes/μL, lymphocytes usually predominate; India ink preparation (budding yeasts with wide capsules; positive in 30-60%) and culture (positive in 40-70%) of CSF; latex agglutination of CSF and serum for antigen (positive in 80-90%); serology (tube agglutination test for antibody positive in ≈ 40%); evaluate inner and middle ear for temporal bone involvement; poor prognosis if markedly positive India ink test, spinal fluid pressure > 300 mm, CSF glucose < 20 g/dL, CSF leucocytes < 20/μL, cryptococci isolated from other sources (eg., blood, urine), no detectable cryptococcal antibody, CSF antigen > 1:32, patient with malignancy or receiving corticosteroids
Treatment: measure opening pressure and consider means to reduce pressure if > 25 cm H_2O; amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 6-10 w (adjust dose according to tolerance) ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 6-10 w (monitor plasma levels); fluconazole 20 mg/kg to 800 mg/kg orally or i.v. initially, then 10 mg/kg to 400 mg daily for at least 10 w (in immunocompromised, follow with fluconazole 5 mg/kg to 200 mg orally daily indefinitely as prophylaxis); itraconazole + flucytosine; intrathecal amphotericin B for patients who relapse or fail to respond or if nephrotoxicity precludes i.v. (many complications of therapy); increased chance of relapse following therapy if no detectable antibody, persistent malignancy and/or corticosteroid therapy; surgical excision of focal brain lesions associated with high mortality; transfer factor (investigational)

Viral Meningoencephalitis

Agents: *Crimean-Congo hemorrhagic fever virus*, *mumps virus* (1:6000 mumps cases), enteroviruses (especially chronic *human echovirus 11* infections in agammaglobulinemic patients), *rubella virus* (rare), *simplexvirus* 1, *Russian spring-summer encephalitis virus*, *human parainfluenza virus 4*, *human adenovirus*
Diagnosis: clinical; CSF examination; serology; isolation of virus from blood, CSF or autopsy specimens

Mumps virus: decreased consciousness, focal neurologic deficits; death rate 0.5-2.3%; protein 146-320 mg/dL, glucose 24-43 mg/dL, 208-774 leucocytes/μL, 2-26% polymorphs, 74-98% lymphocytes, 66-6000 erythrocytes/μL

Treatment: oral prednisone; intraventricular immunoglobulin; supportive

Bacterial Meningoencephalitis

Agents: *Listeria monocytogenes* (≥ 6 d postnatal; may be preceded by septicemia in adult; may mimic tuberculous meningitis), *Brucella*, *Coxiella burnetii*, *Mycoplasma* (rare); also in 2% of cases of Lyme disease
Diagnosis: micro and culture of CSF
Treatment:

Listeria monocytogenes: ampicillin + gentamicin

Brucella: rifampicin 900 mg/d orally for 90 d + cotrimoxazole 5/25 mg/kg/d orally or i.v. for 90 d (add corticosteroid briefly)

Coxiella burnetii, Mycoplasma: doxycycline for 2-3 w

Rabies (Hydrophobia): meningoencephalitis prevalent in Africa, India, Indonesia, Philippines, Mexico; > 50,000 deaths/y worldwide; ≈ 3 cases/y (74% from bats) in USA; few bat-associated cases in Australia; in Europe, 70% of cases are in foxes; in Thailand, 95% are in dogs; transmission by saliva of infected animal; human to human transmission by corneal transplantation recorded; incubation period 10 d to 6 mo; ≈ 100% mortality
Agent: *Lyssavirus*
Diagnosis: no signs or symptoms during incubation period; fever, malaise, anorexia, headache, paresthesias or pain at site of bite during prodrome lasting 2-10 d; agitation, hyperventilation, aphasia, paralysis, hydrophobia (17-50% of cases), pharyngeal spasms, delirium during acute neurological stage lasting 2-7 d; hypotension, cardiac arrhythmia, hypoventilation, pituitary dysfunction, coma, infection, thromboembolism in coma stage which lasts days to weeks; death or recovery (only 2 case reports) after months; CAT scan normal or temporal lobe edema; diffuse, slow, non-focal dysrhythmia in electroencephalogram; fluorescent antibody staining or PCR on corneal impressions (positive in 50% of cases), skin, temporal lobe biopsy, neck biopsy, brain tissue postmortem or after

inoculation of saliva, tissue (Ammon horn of brain) postmortem or CSF into cell culture, mice or suckling mice; light microscopy (hematoxylin-eosin stained sections of tissue postmortem show Negri bodies) and electron microscopy (*Lyssavirus*) of fixed biopsy material; high antibody titres (rapid fluorescent focus-inhibition titres) in serum or CSF; neutralisation antibody titre of CSF (unvaccinated); virus isolation from clinical specimens followed by direct fluorescent antibody testing; CSF protein 85-133 mg/dL, glucose 105-158 mg/dL, 4-6 neutrophils/μL, 6-43 lymphocytes/μL, 8-16 red cells/μL; white cell count increased; possible complications include hydrophobia (spasms of pharynx), seizures, cerebral edema, inappropriate ADH secretion, diabetes insipidus, hypothermia and hyperthermia, arrhythmia, congestive heart failure, hypotension, aspiration, atelectasis, hypoxemia, pneumonia, gastrointestinal haemorrhage

Treatment (All Persons Exposed to a Bite, Scratch or Abrasion Inflicted by a Brain-positive Animal, in an Unprovoked Attack by a Domestic Dog or Cat in a Rabies Area or in a Provoked or Unprovoked Attack by an Escaped Carnivorous Wild Animal in Such an Area): thorough immediate cleansing of wounds with soap solution or detergent and thorough rinsing under running water, followed by 0.1% benzalkonium chloride or other quaternary ammonium detergent or, if unavailable, 70% alcohol or tincture of iodine +:

Unimmunised: rabies immune globulin 20 U/kg, half applied by instillation deep into the wound and half i.m., followed by human diploid cell vaccine 6 doses i.m. on days 0, 3, 7, 14, 28, 90

Previously Immunised: human diploid cell vaccine 2 doses i.m. on days 0 and 3

leave wound unsutured for a few days; give tetanus antiserum and systemic antibiotics

Prophylaxis: highly effective killed vaccine (human diploid cell); 5 doses lead to ≥ 1:16 titre in 100%; no rabies cases have resulted in > 120 persons who have received HDCV and been bitten by rabid animals; pain and swelling at injection site in ≈ 25%, mild systemic (eg., headache, dizziness) in ≈ 20%, 1 reported case of Guillain-Barré syndrome; local or mild systemic reactions should be treated with aspirin; not contraindicated in pregnancy

Prevention and Control: animal immunisation and other control procedures aimed at stray and wild animals

FUNGAL MENINGOENCEPHALITIS

Agent: *Bipolaris* (2 cases in patients with cancer)

Diagnosis: histology and culture of biopsy

Treatment: resection of localised lesions; itraconazole

EOSINOPHILIC MENINGOENCEPHALITIS

Agents: *Angiostrongylus cantonesis* (China, Far East, Hong Kong, Papua New Guinea), *Angiostrongylus malaysiensis* (Malaysia), *Baylisascaris procyonis* (cases in USA from raccoons), *Toxocara, Gnathostoma spinigerum*; also **NEUROCYSTICERCOSIS**, ventriculoperitoneal shunt

Diagnosis: history of exposure to snails, slugs, molluscs; severe headache, nausea, vomiting, paresthesias, low grade or absent fever, cranial nerve abnormalities, moderate to high eosinophilia in CSF and blood; parasite may be recovered from CSF or anterior chamber of eye; serology (*Angiostrongylus* cross-reacts with *Toxocara canis* in ELISA test)

Differential Diagnosis: cerebral cysticercosis (computed tomography), gnathostomiasis (involvement of nerve roots, bloody or xanthochromic CSF, sudden impairment of sensorium due to cerebral hemorrhage), paragonimiasis (chronic hemoptysis, cavities on chest X rays, punctate nodular calcifications on skull X-rays; skin testing, serology of blood and CSF), schistosomiasis (clinical, recovery of *Schistosoma japonicum* eggs from stool), fungal infections (fungal cultures), allergic conditions, multiple sclerosis (characteristic CSF immunoglobulin pattern and chronic clinical course without symptoms of increased intracranial pressure), neurosyphilis (syphilis serology), tuberculous meningitis (mycobacterial culture), Hodgkin's disease (lymphadenopathy, bone marrow involvement, weight loss, night sweats, pruritus, deteriorating course of illness), reaction to foreign bodies (eg., neurological shunts), lymphocytic choriomeningitis (viral culture)

Treatment: dexamethasone + analgesics; death common and neurological deficits usual with *Bayliascaris procyonis*; with other agents, recovery in mild disease is usually spontaneous, but occasionally disease has been fatal

AMOEBIC MENINGOENCEPHALITIS

Agents: *Naegleria fowleri* (primary amoebic meningoencephalitis; rare; acute; probably worldwide in heated water such as swimming pools, warm springs and in brackish water; invasion of CNS via nasal mucosa and olfactory nerve after bathing in amoeba-infested water or inhaling dust contaminated with viable cysts),

Acanthamoeba (granulomatous amoebic meningoencephalitis; rare; more insidious onset and more prolonged course; in chronically ill, diabetic, alcoholic, immunocompromised, immunosuppressed; no history of swimming; route of infection probably hematogenous, with portal of entry primary focus in skin, lung, kidney, eye, grafts), *Balamuthia mandrillaris* (granulomatous amoebic meningoencephalitis; 5 cases in Australia; not yet detected in environment)
Diagnosis: mental status abnormalities, headache, fever, nausea and vomiting, stiff neck, seizures, anorexia, diplopia and blurred vision, photophobia, visual hallucinations, papilledema, cranial nerve palsies, nystagmus, gait ataxia, Babinski's sign, Kernig's sign

Naegleriasis: sudden onset, sore throat, rhinitis, ageusia, parosmia, anisocoria, disconjugate gaze, coma on admission or shortly thereafter; death by cardiorespiratory arrest, pulmonary edema, brain edema

Acanthomoebiasis: sleep disturbances, hearing difficulties, hemiparesis, aphasia, coma at end of clinical course; death from bronchopneumonia and liver or kidney failure
multifocal areas of decreased density in subcortical gray matter, gyriform pattern of enhancement in computerised axial tomography; cerebral angiography normal; wet mount (motile trophozoites 8-15 μm), Giemsa-Wright and modified trichome stains and culture of CSF and pus; amoebic trophozoites on electron microscopy, indirect fluorescent antibody test of brain biopsy (positive in 67% of cases); serology (positive in 50%); white cell count 8000/μL; CSF protein increased, glucose normal or decreased, 20-7300 leucocytes/μL, all mononuclears to predominance of polymorphs
Differential Diagnosis:

***Naegleria*:** bacterial meningitis (including partially treated), early viral meningitis

***Acanthamoeba*:** partially treated bacterial meningitis, viral meningonecephalitis, tuberculous meningitis, fungal meningitis, parameningeal infectious focus, carcinomatous meningitis, CNS vasculitis
Treatment: recovery very rare; amphotericin B 1.5 mg/kg/d i.v. in 2 divided doses then 1 mg/kg/d for 6 d + amphotericin B 1.5 mg intrathecally for 2 d then 1 mg intrathecally on alternate days for 8 d + miconazole 350 mg/m^2 daily i.v. in 3 divided doses for 9 d + miconazole 10 mg intrathecally daily for 2 d then 10 mg intrathecally on alternate days for 8 d + rifampicin 10 mg/kg daily in 3 divided doses for 9 d
ENCEPHALITIS: ≈ 7 cases/100,000 person-years; arboviral, enteroviral, associated with childhood infections (*measles virus*, *mumps virus*, *simplexvirus 3*, *rubella virus*), associated with respiratory infections, other infectious agents (< 1% of total cases, no deaths)
Agents: 70-74% indeterminate (69% of total encephalitis deaths, case-fatality rate 11%); 21-27% of documented cases childhood viral (5% of total encephalitis deaths, case-fatality rate 6%; transmitted by aerosolised droplets; 10% *simplexvirus 3* (also common in impaired cell-mediated immunity), 6-10% *mumps virus* (1:6000 mumps cases; 0.5-2.3% case-fatality rate), 6-7% *measles virus* (33% of measles deaths, 67% of measles deaths in patients > 18 y; 0.6/1000 cases; case-fatality rate 14%), *rubella virus* (< 1% of total cases; 1/5000-1/6000 cases; in 4% of adults with rubella; 20-50% case-fatality rate)), 12-21% *simplexvirus* (15% of total encephalitis deaths, case-fatality rate 40-70% untreated, 10-20% treated with acyclovir; most common cause of sporadic fatal encephalitis in USA; all age groups but usually newborn, children and young adults; whites > blacks; no seasonal predominance; usually reactivation; common in impaired cell-mediated immunity; may result in late persistent or recurrent disease of CNS; 67% of affected neonates with significant neurologic sequelae), 10-53% several arboviruses (6% of total encephalitis deaths; case-fatality rate 4%; transmission by mosquito bite and other arthropods; incubation period 4-21 d; mainly in summer, autumn, early winter; St Louis encephalitis (9% of total cases in USA; 5% of total encephalitis deaths; case-fatality rate 7%; USA, Central America, Caribbean Islands, Colombia, Brazil, Argentina; reservoir birds and bats; vector *Culex* mosquito), California encephalitis (4% of total cases in USA; rare deaths; North-Central USA; reservoir rabbits, squirrels, mice; vector *Aedes* and *Culex* mosquitoes), Western equine encephalitis (3% of total cases in USA; case-fatality rate 10%; all of USA, Canada, Central America, Guyana, Brazil, Argentina; reservoir birds and horses; vector *Culex tarsalis* mosquito), Eastern equine encephalitis (≈ 8 cases/y in USA; case-fatality rate 30-75%; < 1% of total encephalitis deaths; Eastern USA, Central America, Caribbean Islands, Brazil, Guyana, Argentina; reservoir horses (attack rate 18/1000) and birds; vector *Aedes* mosquito; also highly infectious as aerosol, possible biowarfare agent), Japanese B encephalitis (> 50,000 cases/y worldwide; mosquito vector and reservoir; other reservoirs pigs, water birds; attack rate 4/100 000; case-fatality rate > 20%), Venezuelan equine encephalitis (Florida, Texas, Central America, Northern S America; reservoir horse, rodents, dogs, bats, birds; vector *Culex*, *Aedes* and *Deinocerites* mosquitoes; also highly infectious as aerosol (10-100 organisms required for infection), possible biowarfare agent; case-fatality rate 1% but morbidity and mortality may be much higher in biological attack; no person-to-person spread), Powassan

encephalitis (NE and Central Europe, Canada, Northern USA; reservoir rodents; vector tick; case-fatality rate 10-20%), *Russian spring-summer encephalitis virus*, *Rio Bravo virus*, *Murray Valley encephalitis virus*, *Ilheus virus*, *Colorado tick fever virus*, *West Nile virus*, *Bunyavirus La Crosse* (20-30/100,000 children/y in many parts of US Midwest; mainly children < 15 y)), 6% *influenza A virus* (postinfectious encephalomyelitis), 6% *human adenovirus* (especially serotype 7), 3-40% enteroviral (< 1% of total encephalitis deaths, case-fatality rate 6%; 15% *human echovirus 11*, 9% *human echovirus 7*; *human echovirus 2-4, 6, 16, 18, 19, 30*, *Coxsackievirus*, *Poliovirus*, *human enterovirus 71*; infrequent infections in impaired cell-mediated immunity; may cause chronic disease in primary hypogammaglobulinemia), 3% *simplexvirus 3* (4% of total encephalitis deaths, case-fatality rate 50%); infectious mononucleosis (< 1% of total cases; < 1% of total encephalitis deaths), *vaccinia virus* (postvaccination; infrequent infections in impaired cell-mediated immunity), Rift Valley fever (in < 1% of infections), rabies, *JC polyomavirus* (progressive multifocal leucoencephalopathy; infrequent infections in impaired cell-mediated immunity; also in AIDS), *Human cytomegalovirus* (extremely infrequent infections in impaired cell-mediated immunity and in AIDS), *cercopithecine herpesvirus* 1(herpesvirus of monkeys; occasional fatal encephalitis and ascending paralysis in man), *lassa virus*, bunyaviruses, *lymphocytic choriomeningitis virus*, *Nipah virus*, slow infections, rickettsias, *Coxiella burnetii*, *Mycoplasma* (rare), *Chlamydia*, bacteria associated with brain abscess and meningitis, *Listeria monocytogenes* (rhomboencephalitis; nonimmunosuppressed adults; case-fatality rate 51%; sequelae in 61% of survivors), spirochetes, mycobacteria, *Drechslera* (granulomatous), *Cryptococcus neoformans*, *Coccidioides immitis*, *Candida*, *Histoplasma capsulatum*, *Aspergillus*, phycomycetes, *Toxoplasma gondii* (3-40% of AIDS patients), *Trichinella spiralis, Baylisascaris procyonis* (from raccoons)

Diagnosis: fever, neurologic abnormality of recent onset; MRI; culture of blood, CSF, throat washings, rectal swab, urine, fluid from skin lesions, brain biopsy in embyronated eggs, laboratory animals, tissue culture; serology (complement fixation test, microagglutination, indirect fluorescent antibody titre, hemagglutination inhibition, neutralisation); immunofluorescent antibody tests on CSF, brain biopsy; PCR on CSF (HSV, CMV, VZV, EBV, JE, rabies, HIV, enteroviruses, certain arboviruses)

Viral: CSF protein increased in 75% of cases, glucose normal, cells 200-2000/μL, 60-90% neutrophils in early stages, lymphoid pleocytosis in 80% of later cases, erythrocytes or xanthochromia frequently present

Measles:

Acute: recrudescence of fever during convalescence from measles, headache, seizures, changes in mental status; generalised swelling of brain on computerised axial tomography; diminished activity on electroencephalogram; protein increased in 75% of cases, glucose normal, lymphoid pleocytosis in 80% of cases

Atypical: CSF protein 104 mg/dL, glucose 50 mg/dL, 9 leucocytes/μL, 2 erythrocytes/μL

Subacute: 1-7 mo after measles attack; immunocompromised patients (70% acute lymphoblastic leukemia); 100% altered levels of consciousness, 97% seizures (78% focal); histologic and PCR studies of brain tissue

Subacute Sclerosing Panencephalitis (Subacute Inclusion Panencephalitis, Von Brogaert's Disease): rare and fatal; stage 1: ≈ 6 y after attack of measles; subtle changes in intellectual skills, mood swings, inappropriate affect, drooling and changes in speech (less common); stage 2: myoclonic jerks, clumsiness, ataxia, choreoathotosis, ocular changes (cortical blindness, optic atrophy, etc) in ≈ 50%; stage 3: marked mental deterioration, coma, opisthotomus, decerebrate or decorticate posturing, autonomic nervous dysfunction, often death due to infection; stage 4: patient calmer, nearly total loss of cortical function, purposeless responses (eye movements, episodic laughing or crying), severe autonomic nervous dysfunction, death from vasomotor collapse or infection; electroencephalogram (60% 'pseudoperiodic' patterns, 40% atypical alterations); ELISA titres on 1:5 CSF and 1:2000 serum; microscopy, electron microscopy and immunofluorescence of brain tissue

Arboviral: culture of acute phase blood and CSF; serology (paired sera; complement fixation test, hemagglutination, ELISA (IgM), hemadsorption); inoculation of suckling mouse with blood, brain post mortem

St Louis Encephalitis: temporal lobe lesions on computerised axial tomography; protein > 50 mg/dL in 91% of cases, glucose > 45 mg/dL in 81%, leucocytes ≈ 10/μL in 75% of cases, lymphocytes ≈ 50% in 71%

Venezuelean Equine Encephalitis:

Influenzal: only constitutional symptoms, febrile course 1-4 d

Fulminant: short febrile course with rapid progression to shock, coma and convulsions, disseminated intravascular coagulation; survivors often have sequelae

Encephalitic: fever for 2 w or more, sometimes diphasic; CNS symptoms and signs develop during latter phase; usually no sequelae

Eastern Equine Encephalitis: may have influenzalike prodrome with fever, headache, vomiting, malaise and, rarely, relatively mild encephalitic phase with somnolence but, more commonly, abrupt illness with high fever, convulsions and rapidly progressive coma; may exhibit diffuse or focal signs mimicking herpes encephalitis; magnetic resonance imaging

West Nile Virus: oculomotor abnormalities, movement disorders, myoclonus, features of Parkinson's disease; isolation from tissue, blood, CSF, other body fluid; PCR on tissue, blood, CSF, other body fluid; IgM capture EIA on CSF or serum; plaque reduction neutralising antibody titre on serum or CSF (> 4X change in paired, appropriately timed specimens); EIA for IgM + EIA or HI (confirmed by plaque reduction neutralising antibody titre) in single serum specimen

Bunyavirus La Crosse: fever in 86%, headache in 83%, vomiting in 70%, seizures in 46%, disorientation in 42%; indirect immunofluorescence of serial IgM and IgG titres

Simplexvirus: focal neurologic signs in 85-90%, fever in 80-95%, headache in 55-70%, stiff neck in 45-55%, herpes labialis in 15-20%; CSF abnormal in 85-100%, 10-100 leucocytes/μL in 80-100%, > 10 erythrocytes/μL in 66-75%, elevated protein in 55-90%, hypoglycorrhachia in 0-25%; localised findings on EEG, brain scan or arteriogram, usually localised to temporoparietal lobe, in 60-95%; MRI—T2 prolongation or gyriform enhancement of medial temporal lobe, insular cortex or cingulate gyrus, petechial hemorrhage of temporal or orbitemporal lobes, effacement of adjacent CSF spaces; PCR on CSF; brain biopsy positive in ≈ 90% and may discover another treatable cause—cryptococcal meningoencephalitis, tuberculosis, brain abscess, brain tumour

Enteroviral: virus isolation; PCR

Mumps virus: virus isolation

Nipah virus: associated with pigs in Malaysia and Singapore; headache, drowsiness, fever; low lymphocyte counts in 82%, high levels of CSF protein in 73%, elevated white blood cell counts in 64%, low platelet counts, low serum sodium levels and elevated aspartate aminotransferase in 46%; MRI (small lesions primarily within white matter, with transient punctate cortical hyperintensities on T1-weighted images); immunohistochemistry + serology

Listeria monocytogenes: prodrome of headache, nausea or vomiting and fever, lasting several days, followed by progressive asymmetrical cranial nerve palsies, cerebellar signs, hemiparesis or hypesthesia and impairment of consciousness; culture of blood (61% positive), CSF (41% positive); magnetic resonance imaging

Mycoplasma pneumoniae: 78% meningeal signs/symptoms, 53% temperature ≥ 39°C

Trichinosis: enlarging areas of hemorrhage in parietal regions on computerised axial tomography

Toxoplasma: focal or generalised neurologic abnormalities; contrast-enhanced computerised axial tomography (ring or nodular enhancement in > 90%); magnetic resonance imaging; serology (IgG and IgM); Giemsa-Wright stained smears of centrifuged sediment of CSF or brain aspirate, or impression smears of brain biopsy

Treatment:

Measles: ribavirin 20 mg/kg/d i.v.

Simplexvirus, ***Nipah virus***:

Neonates: aciclovir 20 mg/kg i.v. 8 hourly for 21 d (adjust dose for renal function)

Others: aciclovir 10 mg/kg i.v. 8 hourly for at least 14 d (adjust dose for renal function)

Chlamydia, ***Mycoplasma***, ***Rickettsia***: i.v. doxycycline

Toxoplasma: pyrimethamine 2 mg/kg to 50-100 mg orally as loading dose then 1 mg/kg to 50 mg orally daily + sulphadiazine 50 mg/kg to 1-1.5 g orally or i.v. 6 hourly or clindamycin 15 mg/kg to 600 mg orally or i.v. 6 hourly if allergic to sulphonamides + calcium folinate acid 15 mg orally daily (to reduce incidence of bone marrow suppression) for 3-6 w; 5-fluorouracil; spiramycin

Maintenance Therapy in HIV/AIDS: pyrimethamine 25-50 mg orally daily + sulphadiazine 500 mg orally 6 hourly or 1 g orally 12 hourly or clindamycin 600 mg orally 8 hourly if hypresensitive to sulphonamides

St Louis Encephalitis: interferon α-2b

Others: see under **MENINGITIS** and **BRAIN ABSCESS**

Prophylaxis:

Varicella-zoster in Patients with Leukemia, Congenital or Acquired Immunodeficiency, < 24 mo after Haemopoietic Stem Cell Transplant, on Immunosuppressive Medication or with Chronic Graft-versus-host Disease, or Newborn of Mother with Varicella: varicella-zoster immune globulin 625 U i.m. within 96 h of exposure to varicella or zoster from household contact, playmate contact (> 1 h play indoors), hospital contact (in same 2-4 room bedroom or adjacent beds in a large ward), or newborn whose mother contracted varicella 5 d before delivery or within 48 h of delivery), if negative or unknown prior disease history and age < 15 y; live attenuated vaccine (all susceptible health care workers, household contacts and family members ≥ 12 mo and not pregnant or immunocompromised; 85% effective)

Japanese B Encephalitis: effective vaccine

***Toxoplasma gondii* in HIV/AIDS CD4 Count < 200/µg:** cotrimoxazole 80/400 or 160/800 mg daily or 160/800 mg orally 3 times weekly

ENCEPHALITIS LETHARGICA: epidemics in 1920s, sporadic cases reported in recent years

Agent: *influenzavirus*

Diagnosis: Parkinsonian signs in a young person after influenza

Treatment: ? steroids

NONINFECTIOUS NONTYPHOIDAL *SALMONELLA* ENCEPHALOPATHY

Agent: non-typhoidal *Salmonella*

Diagnosis: diffuse and rapidly progressive brain dysfunction and circulatory failure following enteritis; elevated CSF opening pressure, minimal ischemic damage and mild edema on brain CT, slow waves on EEG, microvesicular fatty change in liver, severe enterocolitis

Treatment: supportive

ENCEPHALOMYOCARDITIS

Agent: *encephalomyocarditis virus*

Diagnosis: on symptoms; exposure to rodents

Treatment: non-specific

NEUROSYPHILIS: generalised or focal seizures; stroke; changes in personality, affect, sensorium, intellect, insight, judgment; hyperactive reflexes; Argyll-Robertson pupil; optic atrophy; ataxia; impotence; bladder disturbances; peripheral neuropathy; Romberg's sign; cranial nerves II-VII involvement

Agent: *Treponema pallidum subsp pallidum*

Diagnosis: see **SYPHILIS**

Treatment: benzylpenicillin 3-4 MU i.v. 4 hourly or 18-24 MU/d as continuous infusion for 10-14 d, procaine penicillin 2.4 MU i.m. once daily + probenecid 500 mg orally 4 times a day for 10-14

NEUROCYSTICERCOSIS: 12% of admissions to neurological wards and leading cause of acquired epilepsy in adults in Central and South America, sub-Saharan Africa, east and south Asia; > 50,000 deaths/y; 58% parenchymal calcifications, 48% arachnoiditis, 26% hydrocephalus secondary to meningeal inflammation, 13% parenchymal cysts, 4% hydrocephalus secondary to meningeal fibrosis, 2% brain infarction secondary to vasculitis, 1% mass defect due to large cyst or clump of cysts, 0.7% intraventricular cysts, 0.7% spinal cysts, rare optic nerve

Agent: *Taenia solium*

Diagnosis: epilepsy in 70%; CSF monocytes 300-5000/µL, protein 50-1600 mg/dL, glucose low in 18%; computed tomography; magnetic resonance; IgG and IgM ELISA (sensitivity 87%, specificity 95%) and complement fixation test (sensitivity 22-83%) on CSF; histology of biopsy from brain or spinal cord

Treatment:

Intraventricular Cyst, Spinal Cysts: surgical extirpation (+ ventricular shunt with intraventricular cyst)

Parenchymal Cysts, Vasculitis and Encephalitis, Arachnoiditis, Intraocular Cysts: albendazole 15 mg/kg/d for 1 mo, praziquantel 50 mg/kg/d for 2 w; + antiepileptic drugs if epilepsy; + dexamethasone 24-32 mg/d in vasculitis and encephalitis; + ventricular shunt in arachnoiditis with hydrocephalus; + periocular methylprednisolone acetate 80 mg every 30-60 d and aspiration of intravitreous cysts in intraocular cysts

Granulomas or Calcifications: symptomatic treatment (eg, antiepileptic drugs)

Hydrocephalus Due to Basal Fibrosis: ventricular shunt

Cranial Nerve Dysfunction Due to Basal Fibrosis: specific treatments (eg, surgery for diplopia)

Optic Nerve: dexamethasone sodium phosphate 100 mg i.v. daily for 3 d then oral steroids

CEREBRAL COENUROSIS

Agent: *Multiceps* species

Diagnosis: paraplegia and hemiplegia or leptomeningitis

Treatment: usually fatal

CEREBRAL SPIROMETROSIS

Agent: *Spirometra*

Diagnosis: computed tomography and MRI, followed by stereotactic biopsy

Treatment: surgical resection

CEREBRAL MALARIA

Agent: *Plasmodium falciparum*

Diagnosis: clinical manifestations of acute falciparum malaria; coma, convulsions, other neurological signs and symptoms (particularly inability to localise a painful stimulus) compatible with an acute diffuse meningitis or with an encephalitic process; peripheral asexual *Plasmodium falciparum* parasitemia

Treatment: see **MALARIA**; often fatal

BRAIN ABSCESS AND SUBDURAL EMPYEMA: ≈ 1 case/100,000 person-years; case-fatality rate 10-22% (90% if comatose, 80-90% if rupture into ventricles, 70-100% if multiple, 100% if distant source of infection, 51-53% in pituitary infection); may spread from nearby tissue such as paranasal sinuses, ear and mastoid process, or by metastatic spread from distant organs following, eg, trauma

Agents: 61% *Staphylococcus aureus* (common after trauma or surgery), 18% aerobic Gram negative bacilli (including *Haemophilus aprophilus* and enterics (common with site of origin in ear or paranasal sinuses; *Citrobacter diversus* in neonates; *Klebsiella pneumoniae* hematogenous spread, frequent in diabetics); uncommonly, *Salmonella*, *Actinobacillus actinomycetemcomitans*; rarely, *Brucella melitensis, Haemophilus parainfluenzae, Enterobacter agglomerans, Pasteurella multocida* (infants and adults), *Haemophilus paraprophilus*, *Streptobacillus moniliformis*, anaerobic *Campylobacter*), 8% streptococci (including *Streptococcus milleri*, *Streptococcus sanguis* in intermittently treated jaw infections; occasionally, *Streptococcus pneumoniae*; hematogenous spread, paranasal sinusitis), 2% anaerobes (nontraumatic; especially *Peptostreptococcus* and *Propionibacterium*; also *Actinomyces, Prevotella bivia*), 2% *Staphylococcus epidermidis; Nocardia asteroides* (in impaired cell-mediated immunity), *Listeria monocytogenes* (especially in leukemia and renal transplant recipients; case-fatality rate 57%), *Mycobacterium tuberculosis, Actinomyces pyogenes, Corynebacterium equii* (heart transplant recipient), any vascular pathogen secondary to bacteremia (especially in neutropenics), *Aspergillus* (in neturopenics), *Mucor* (in neutropenics), *Absidia* (in neutropenics), *Rhizopus* (in neutropenics), *Pseudallescheria boydii* (in malignant lymphoma and immunosuppression), *Exophila dermatitidis, Fonsecaea pedrosoi, Dactylaria constricta, Bipolaris hawaiiensis, Bipolaris spicifera, Curvularia pallescens, Cladophialophora bantiana, Rhinocladiella atrovirens* (1 case in HIV-infected i.v. drug abuser), *Curvularia lunata* (rare), *Scedosporium apiospermum* (in immunosuppressed), *Entamoeba histolytica* (amoebic brain abscess usually arises from hematogenous spread of causative organism from lungs or liver; fatal), *Toxoplasma gondii* (in impaired cell-mediated immunity)

Diagnosis: headache in 70%, fever in 50%, retarded consciousness in 50%, papilledema in 50%, focal neurologic deficits in 40%, seizures in 25%, nuchal rigidity rare; culture and histology (Gomori's methenamine silver or PAS shows broad, septate hyphae in mycetoma; Brown and Breen modification of Gram stain shows Gram positive filamentous or branching rods in actinomycetoma, and cocci, coccobacilli or bacilli in botryomycosis) of biopsy; blood cultures; computerised axial tomography (≈ 100% accurate); radionuclide scan (≈ 100% accurate); do not do lumbar puncture (risk of cerebral herniation; CSF, if obtained, will show protein 20-600 mg/dL, glucose 16-93 mg/dL, 0-2300 leucocytes/μL, 30-100% polymorphs); agglutinations; analysis of pus from primary organ and obtained by aspiration or biopsy of abscess

Fungal: Fontura-Masson stained histology and culture of biopsy

Pituitary Gland Infection: headache in all cases, fever in 75% of tuberculous and 100% of other bacterial infections, visual disturbances in all tuberculous and 88% of other bacterial infections, associated tumour or cyst in 94%, sellar erosion or enlargement in 63% of tuberculous and 90% of other bacterial infections, associated sphenoid sinusitis in 89%, abnormal carotid angiogram in 50% of tuberculous and 86% of other bacterial infections, hypopituitarism in 80% of tuberculous and 73% of other bacterial infections, abnormal

pneumoencephalogram in 50% of tuberculous and 75% of other bacterial infections; smear and culture usually negative in tuberculous, positive in 55% of other bacterial infections; > 10,000 leucocytes/μL in all tuberculous and 21% of other bacterial infections

Treatment: surgical drainage or excision; benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly +metronidazole 12.5 mg/kg to 500 mg i.v. 8 hourly + ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly or cefotaxime 50 mg/kg to 2 g every 6 h

Post Neurosurgery: vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly + ceftazidime 50 mg/kg to 2 g i.v. 8 hourly or meropenem 40 mg/kg to 2 g i.v. 8 hourly

From Frontal Sinuses, Teeth: metronidazole + cefotaxime

From Ear and Mastoid: amoxicillin + metronidazole

Secondary to Penetrating Trauma: penicillin + cefotaxime

Metastatic: penicillin + cefotaxime + metronidazole

Staphylococci: fusidic acid 20 mg/kg i.v. 12 hourly as 2 h infusion + clindamycin 600 mg i.v. 8 hourly (child: 15-40 mg/kg i.v. daily in divided doses)

***Nocardia asteroides*:** cotrimoxazole 4/20 mg/kg to 160/800 mg i.v. or orally 6 hourly for 3-4 w, then orally 12 hourly for 3-6 mo

Streptococcus pneumoniae:

Penicillin MIC ≤ 0.125 mg/L: benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 10 d

Penicillin MIC > 0.125 mg/L: ceftriaxone or cefotaxime + vancomycin or rifampicin

Other Streptococci, *Actinomyces*: high dose benzylpenicillin

***Listeria monocytogenes*:** cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

***Haemophilus*:** cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7-10 d, ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 7-10 d, amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7-10 d (if susceptible)

***Brucella*:** cotrimoxazole

Other Aerobic Gram Negative Bacilli: chloramphenicol

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 12 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 12 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (12 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 12 mo) + corticosteroids for first few weeks

Anaerobes: benzylpenicillin 2.4 g i.v. 4-6 hourly + metronidazole 500 mg i.v. infused over 20 minutes 8 hourly, chloramphenicol 1 g i.v. 6 hourly

Fungi:

Bipolaris*, *Rhinocladiella atrovirens: resection; itraconazole

Others: amphotericin B + flucytosine; decompression of spinal cord essential in management of epidural abscess

***Entamoeba histolytica*:** metronidazole

***Toxoplasma gondii*:** sulphadiazine 50 mg/kg to 1-1.5 g orally or i.v. 6 hourly + pyrimethamine 2 mg/kg to 50-100 mg orally initially then 1 mg/kg to 25-50 mg orally daily + calcium folinate 15 mg orally daily for 3-6 w

Sulphonamide Hypersensitive: clindamycin 600 mg orally or i.v. 6 hourly + pyrimethamine as above

Maintenance Therapy in HIV/AIDS: pyrimethamine 25-50 mg orally daily + suphadiazine 500 mg orally 6 hourly or 1 g orally 12 hourly or if hypersensitive to sulphonamides clindamycin 600 mg orally 8 hourly

Prophylaxis *(Toxoplasma gondii* in HIV/AIDS CD4 Count < 200/μL): cotrimoxazole 80/400 or 160/800 mg orally daily or 160/800 mg orally 3 times weekly

Epidural Abscess: 0.2-2 episodes/10,000 hospital admissions; frequently associated with adjacent osteomyelitis or disc infection

Agents: 63-79% *Staphylococcus aureus,* 4% *Streptococcus pneumoniae*, 4% *Streptococcus viridans,* single report of *Streptococcus pyogenes;* also other organisms causing osteomyelitis

Diagnosis: spinal ache, root pain, weakness (including bowel and bladder dysfunction), paralysis, focal neurologic deficits rare; MRI or CT with contrast medium; blood cultures positive in 62%; Gram stain and culture of operative material or aspiration; lumbar puncture contraindicated

Treatment: urgent surgery essential; di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin 4-6 mg/kg (child < 10 y: 7.5 mg/kg; ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function)

Raised Intracranial Pressure

Agent: *Echinococcus granulosus* (hydatid cyst)

Diagnosis: X-ray; serology; exposure to dogs

Treatment: surgery ± albendazole 7.5 mg/kg to 400 mg orally 12 hourly (not < 6 y)

Cerebrospinal Fluid Shunt Infections

Agents: *Staphylococcus epidermidis, Staphylococcus aureus,* streptococci, *Enterococcus*, aerobic Gram negative bacilli, diphtheroids, *Propionibacterium*, *Haemophilus influenzae*, *Pseudomonas*

Diagnosis: fever, evidence of increased intracranial pressure, abdominal pseudocyst; culture of CSF and peritoneal fluid

Treatment: externalisation of peritoneal catheter + intraventricular and systemic antibiotics and later replacement of catheter

Staphylococci: vancomycin 10-20 mg intrashunt daily + rifampicin 10 mg/kg orally 12 hourly + cotrimoxazole 5 mg/kg orally 8 hourly or vancomycin 15 mg/kg i.v. 8 hourly

***Enterococcus faecalis* and Streptococci with Penicillin MIC ≥ 0.2 mg/L:** vancomycin 10-20 mg intrathecal daily + 15 mg/kg i.v. 8-12 hourly + gentamicin 8 mg intrathecal daily

Streptococci with Penicillin MIC ≤ 0.1 mg/L: gentamicin 8 mg intrathecal daily + i.v. benzylpenicillin

Aerobic Gram Negative Bacilli: gentamicin 8 mg intrathecal daily + cefotaxime 50 mg/kg i.v. 12 hourly to 30 mg/kg 4 hourly

Diphtheroids and *Propionibacterium*: intrathecal vancomycin 10-20 mg daily + i.v. vancomycin 15 mg/kg 8-12 hourly or cotrimoxazole 15 mg/kg orally 8 hourly

Guillain-Barré Syndrome (Acute Polyradiculoneuritis): symmetrical ascending paralysis, usually self-limited and reversible but 5-10% fatal; 1-2 cases/100,000; 0.7 deaths/million doses of influenza vaccine

Agent: *influenza A virus*, *hepatitis B virus*, *human cytomegalovirus*, *Epstein-Barr virus*, *simplexvirus 3, rubella virus, human immunodeficiency virus, mumps virus* (rare), *HIV*, *Campylobacter jejuni*, *Mycoplasma pneumoniae, Plasmodium falciparum*

Diagnosis: acute or subacute onset of distal paraesthesia, weakness and muscle pain, with tendency for proximal spread over 2 w and with albuminocytologic dissociation in CSF; fever absent at onset of paralysis, meningeal irritation usually absent, residual paralysis usually absent, sensation may be diminished (cramps, tingling, hypesthesia of palms and soles), deep tendon reflexes diminished but may return in several days

Differential Diagnosis: poliomyelitis (high fever always present at onset of flaccid paralysis, severe myalgia and backache, dysautonomia, inflammatory CSF, abnormal electromyogram at 3 w, severe asymmetrical atrophy at 3 mo), traumatic neuritis (pain in gluteus, hypothermia, frequent blood pressure alterations, sweating, blushing and body temperature fluctuations, CSF normal, symmetrical atrophy of peroneal muscles at 3 mo), transverse myelitis (anesthesia of lower limbs with sensory perception, hypothermia in affected limb, CSF normal to mild increase in cells, moderate atrophy of affected lower limb at 3 mo)

Treatment: none specific

Acute Paralytic Poliomyelitis: 1948 laboratory confirmed cases in 2005; Afghanistan, India and Pakistan major reservoirs; eradicated in Western Hemisphere in 1994; last notification of wild poliovirus infection in USA in 1979 and in Australia in 1986; transmission fecal and respiratory; incubation period 1-3 w, latent period 1-3 d, infectious period 14-20 d, interepidemic period 2-5 y

Agents: *human poliovirus 1-3*; also some coxsackieviruses (sustained paralysis with *human coxsackievirus A4*, *A7*, *A9, echo 9 virus*, transient paralysis with *human coxsackievirus A2, B2-B5*), *human echovirus 1, 2, 4, 6, 7,11, 16, 18, 30*, *human cytomegalovirus* in AIDS, *West Nile virus*

Diagnosis: 95% asymptomatic; 4-5% mild febrile illness (upper respiratory tract infection, gastrointestinal illness, flulike illness); 1-2% mild prodromal illness followed by aseptic meningitis; <1% acute flaccid paralysis; fever at onset of paralysis, meningeal irritation (stiff neck, headache, vomiting) usually present, severe pain in muscles, backache, paralysis usually asymmetrical, progression of paralysis 3-4 d, residual paralysis usually present, paresthesia rare, sensation normal, deep tendon reflexes diminished or absent, electromyogram at 3 w abnormal, severe asymmetrical atrophy at 3 mo, skeletal deformation developing later; spinal disease 79% of cases, bulbar 2%, combination 19%; case-fatality rate for paralytic illness 2-5% in children, 15-30% in adults and 25-75% in bulbar disease; viral culture of feces or rectal swab (2 specimens at least 24 h apart) or spinal cord, grey matter, medulla, pons, cerebrum, Peyer's patches, intestinal contents post mortem (within 24 h of death) in monkey or human cell culture; CSF protein 38-154 mg/dL, glucose 81 mg/dL, 10-335 leucocytes/μL, 5% polymorphs, 80% lymphocytes, 15% monocytes, 9 erythrocytes/μL; neutralisation antibody titre or complement fixation test on serum (≥ 4X increase or ≥ 1:512)
Differential Diagnosis: Guillain-Barré syndrome (fever not common, cramps, tingling, hypesthesia of palms and soles, CSF albumin-cytological dissociation, normal EMG at 3 w, mild sequelae at 3 mo), traumatic neuritis (pain in gluteus, hypothermia, frequent blood pressure alterations, sweating, blushing and body temperature fluctuations, CSF normal, EMG normal at 3 w, symmetrical atrophy of peroneal muscle at 3 mo), transverse myelitis (fever rarely present, anesthesia of lower limbs with sensory perception, hypothermia in affected limb, CSF normal or mild increase in cells, EMG normal at 3 w, moderate atrophy in affected limb at 3 mo)
Treatment: non-specific
Prophylaxis (*human poliovirus*): oral vaccine phased out in USA by 2000 because of continued vaccine-associated paralytic poliomyelitis, but is still recommended for mass vaccination during polio outbreaks; all infants and children, incompletely vaccinated children, travellers to areas or countries where polio is epidemic or endemic, immuncompromised individuals, communities or population groups with disease caused by wild poliovirus, laboratory workers who handle poliovirus specimens, healthcare warkers who have contact with patients excreting wild poliovirus, and unvaccinated adults whose children will receive oral poliovirus vaccine should receive 4 doses inactivated vaccine (contraindicated if severe febrile illness, allergy to streptomycin or neomycin, vomiting or diarrhoea, some malignant conditions, *HIV* infection in individual or household contacts, pregnant woman in first 4 months of gestation); vaccine 90-100% efficacy, lifetime immunity, marginally cost effective
Post-polio Syndrome: development of new muscle weakness and fatigue in skeletal or in bulbar-controlled muscles, unrelated to any known cause, that begins between 25 and 40 y after an acute attack of paralytic poliomyelitis; occurs in 25-40% of survivors infected in childhood
Agent: *human poliovirus*
Diagnosis: history of acute paralytic poliomyelitis in childhood or adolescence; history of partial recovery of motor function and maintenance of function for at least 15 y; residual muscle atrophy in at least one limb, accompanied by weak or missing reflexes but normal sensation; normal functioning of sphincter muscle
Treatment: supportive
Botulism: paralytic illness caused by neurotoxin; associated with home-canned foods with low acid content, improperly canned commercial foods, home-canned or fermented fish or other marine or freshwater animals, herb-infused oils, baked potatoes in aluminium foil, cheese sauce, bottled garlic, foods held warm for extended periods; 0.5% of foodborne disease outbreaks in USA, 0.1% of cases, 3% of deaths; 226 cases from 114 outbreaks in Alaska in 1950-2000 (all from fermented foods); last case in Australia in 1998; also inhalational
Agent: *Clostridium botulinum*
Diagnosis: incubation period 2 h - 10 d (usually 12-36 h); vomiting, diarrhoea; developing cranial nerve paralysis causing blurred vision, ptosis, mydriasis, diplopia, dilated and fixed pupils, dysphonia, dysphagia and dry throat; dysarthria, symmetrical, descending, progressive skeletal muscle weakness, respiratory impairment, motor palsy, diffuse flaccid paralysis follow; sometimes postural hypotension; patient alert and afebrile; duration of illness days to months; electromyogram with rapid repetitive stimulation of affected area at 20-50 Hertz, tensilon test, CSF protein normal, computerised tomography scan of head, magnetic resonance imaging; ELISA test for botulinum toxin in serum, stool and food or from swab of nares; mouse bioassay
Differential Diagnosis: Guilllain-Barré syndrome, myasthenia gravis, poliomyelitis, tick paralysis, cerebral vascular accident, heavy metal (thallium, arsenic, lead) or organophosphate toxicity
Treatment: supportive + antitoxin (no deaths if early diagnosis)
Prophylaxis: passive with antitoxin or active with toxoid

AIDS Dementia Complex (HIV Encephalopathy)
Agent: *human immunodeficiency virus*
Diagnosis: 'subcortical dementia' with slowing of mental and motor functions, diffuse cognitive impairment, behavioural torpor, in *human immunodeficiency virus* positive individual; computed tomography and magnetic resonance imaging; CSF examination
Treatment: zidovudine
Tick Paralysis: case-fatality rate 10%
Agents: various hard tick species (*Ixodes holocyclus* in Australia, *Dermacentor andersoni* in southern and western USA, *Dermacentor variabilis* and *Amblyomma americanum* in southern and eastern USA)
Diagnosis: weakness, pulmonary complication (respiratory failure; bilateral raised hemidiaphragms on chest X-ray); presence of tick; history; CSF protein and cell count normal; compound action potentials of nerves and associated muscles decreased, nerve conduction velocity decreased
Treatment: tick removal; usually supportive only, but antitoxin may be given
Kuru: age > 4 y, insidious onset, dementia ±, sensory defects ±; mainly women and children of an isolated tribe (Fore) in Papua-New Guinea; transmitted by eating infected brain tissue in ritual ceremony for dead tribal member
Agent: prion
Diagnosis: clinical (ambulant stage: subjective unsteadiness, ataxic gait, convergent strabismus, shivering-like truncal tremor, dysarthria; sedentary stage: needs support for walking, rigidity of limbs, clonus, emotional lability with outbursts of pathologic laughter, no mental deterioration or sensory changes; terminal: unable to sit without support, urinary and fecal incontinence, bulbar signs, inanition, decubitus ulcers, pneumonia)
Treatment: none
Creutzfeldt-Jakob Disease: age > 18 y (average 63 y), insidious onset, dementia and sensory defects present; disease duration 1 mo - 10 y; inherited form with worldwide incidence ≈ 1:1,000,000 and apparently infectious form
Agent: prion
Diagnosis: muscular spasms, reduced mental function, loss of higher brain function, abnormal behaviour; periodic sharp waves in EEG in 65-70%; CSF 14-3-3 protein in ≈ 90%; histology
Treatment: none
Variant of Creutzfeldt-Jakob Disease: form associated with bovine spongiform encephalopathy, occurring in younger patients
Agent: prion
Diagnosis: psychiatric signs, depression or schizophrenia, stickiness of the skin, instability, walking difficulties, involuntary movements, prostration and death; median age at death 29 y; pulvinar sign (high T2 signal in posterior thalamus on magnetic resonance imaging; ≈ 75% of cases); no periodic sharp waves on EEG; CSF 14-3-3 protein in 50%; histology of tonsils (presence of disease-associated glycoforms of protease-resistant prion protein)
Treatment: none; possible benefit from quinacrine, chlorpromazine
Gerstman-StrÄussler-Scheinkers Disease: discoordination followed by increasing dementia; ≈ 50 families affected; inheritance of PrP gene mutation involved
Agent: prion
Treatment: none
Fatal Familial Insomnia: sleep problems and autonomic nervous system manifestations, followed by full-blown insomnia and dementia; described in 9 families; inheritance of PrP gene mutation involved; disease lasts about 1 y
Agent: prion

Chapter 7

Skin Infections

SKIN INFECTIONS: Many skin infections are primarily a result of irritation, allergy, hypersensitivity, or a reflection of systemic disorders. Nonetheless, there are a considerable number of primary skin infections which are commonly encountered, and bacterial and fungal superinfection is common. Patient history is essential for meaningful investigation.

LOCALISED SKIN LESIONS

Agents: *simplexvirus*, *human papillomavirus*, molluscum contagiosum (2% of male sexually transmitted disease, 0.6% of female), cowpox (from cattle), orf (contagious pustular dermatitis; from sheep; rare in man), paravaccinia (milker's nodes, milker's nodules, pseudocowpox; from cattle), *human echovirus 25* and *32* (hemangioma-like lesions), *Streptococcus pyogenes*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Francisella tularensis*, *Clostridium botulinum, Listeria monocytogenes* (rare), Gram negative bacilli (*Aeromonas hydrophila* (often fatal), *Vibrio parahaemolyticus*, *Escherichia coli*, *Pseudomonas aeruginosa* (ecthyma gangrenosum), *Serratia marcescens, Proteus, Klebsiella*), *Staphylococcus aureus, Corynebacterium jeikeium, Rickettsia, Blastomyces dermatitidis, Candida, Drechslera* (in neutropenia), *Rhizopus, Aspergillus, Mucor, Leishmania tropica* (anthroponotic cutaneous leishmaniasis, dry cutaneous leishmaniasis, urban cutaneous leishmaniasis), *Leishmania major* (rural cutaneous leishmaniasis, wet cutaneous leishmaniasis, zoonotic cutaneous leishmaniasis), *Leishmania aethiopica* (Cuncir, diffuse cutaneous leishmaniasis, Ghisua, leishmaniasis diffusa, lepromatous leishmaniasis), *Leishmania mexicana* (New World cutaneous leishmaniasis), *Leishmania braziliensis* complex, *Leishmania donovani* (rare), *Prototheca;* also painless vesicles in Mucha-Haberman disease

Diagnosis: viral culture of vesicle fluid; direct fluorescent antibody staining or cytological examination of scraping from base of vesicle or other cellular material (herpes: Tzanck smear using Paragon Multiple stain rapid, simple, inexpensive and easy to interpret but sensitivity only 50%), vesicle fluid or pus (cowpox: virions and cytoplasmic inclusions), aspirate, puncture, biopsy (tularemia, leishmaniasis); immunofluorescence; electron microscopy (warts); bacterial and fungal culture of swab of lesions; histology of biopsy; blood cultures; serology

Simplexvirus: creams, ointments, lotions, ice, alcohol, vaginal sprays and sitz baths may reduce viral yield significantly and should be avoided; vesicular lesions should be sampled if possible, a swab for culture and scrapings from the base of the lesion for microscopy being collected, after opening with a sterile hypodermic needle; with ulcerative lesions, any pus should first be removed with a sterile swab; crusts from dried lesions may be lifted with a sterile needle and the same procedure followed; eczema herpeticum potentially life-threatening (hepatitis, disseminated intravascular coagulation) herpetic superinfection of preexisting skin disease

Molluscum Contagiosum: chronic, proliferative epithelial lesions

Cowpox: self-limited, localised vesicular lesions

Orf (Contagious Ecthyma): small, firm, reddish blue papule enlarging to form hemorrhagic pustule or bulla 2-5 cm in diameter, with central crust surrounded by greyish white or violaceous ring, surrounded in turn by zone of erythema; on hand (95%), face or eyelids; history of exposure to sheep or goats; electron microscopy of material from crust or biopsy; rise in antibody by ELISA or Western blot

Paravaccinia: smooth or warty painless lesions and mild systemic complaints

Streptococcus pyogenes: vesicles, forming crusts, especially in children

Neisseria meningitidis: purpuric, petechial or maculopapular lesions containing bacteria

Francisella tularensis: papules resembling insect bites becoming necrotic, ulcerating

Clostridium botulinum: small subcutaneous, non-erythematous, non-tender cyst

Gram Negative Bacilli: cutaneous bullae, erythema multiforme and peripheral lesions in septicemia and endocarditis

Ecthyma Gangrenosum: may be first manifestation of systemic infection (often, bacteremia and sepsis); initial localised edema, rapidly developing to erythematous, usually painless or slightly tender macules 2-3 cm diameter, which progress to indurated subcutaneous nodules over 12–18 h and then vesiculate, with the vesicular fluid often hemorrhagic, slough the vesicle roof to form a deep ulcer with dark central necrosis and violaceous rim expanding into surrounding tissue, and finally may coalesce to form lesions up to 5 cm diameter and covered by a black eschar; histology and culture of skin biopsy; blood cultures

Corynebacterium jeikeium: hemorrhagic or erythematous papular rash, often tissue abscess, necrotic soft tissue lesion

Rickettsia: multiple purpuric lesions in seriously ill patients

Ajelloomyces dermatitidis: papule or pustule developing into granuloma; lesions contain organisms

Candida: macropapular lesions in disseminated candidiasis

***Rhizopus*:** vesiculo-pustular eruptions

Leishmaniasis: examination of smears of tissue or aspirate from lesion or biopsy of ulcer to reveal amastigote; culture of tissue or exudate; erythrocyte count and hemoglobin may be decreased

***Leishmania tropica* Complex:** small raised papules, usually ulcerating to form crusted sores; infectious; Middle East, India, Mediterranean, North Africa; gerbil, dog and human reservoirs; sandfly (*Phlebotomus*) vector

Leishmania tropica: dry ulcer

***Leishmania major*:** faster-growing wet ulcer

***Leishmania aethiopica*:** usually multiple lesions (simple or diffuse)

***Leishmania mexicana*:** Mexico, British Honduras, Amazon River Basin; forest rodent reservoir; sandfly (*Lutzomyia*) vector; similar to leishmaniasis due to *Leishmania tropica* complex but infection with *Leishmania mexicana* often results in destruction of ear cartilage (bahia ulcer, bay sore, chiclero sore, chicle ulcer, ulcera de los chicleros)

Leishmania braziliensis Complex: forest rodent reservoir in Central and South America, dog reservoir in Peru

Leishmania braziliensis: single or multiple ulcers that seldom heal spontaneously

***Leishmania braziliensis guayanensis* (Forest Yaws, Pian Bois):** single lesion or many crateriform ulcers over body, lymphadenitis as result of metastasis along lymphatics

Leishmania panamensis: single crateriform ulcer or a few such ulcers; metastasis may occur along lymphatics

***Leishmania peruviana* (Uta):** single lesion or a limited number of lesions, which usually heal spontaneously; occurs mainly in children; not associated with forest areas

Leishmania donovani: primary cutaneous lesions rare; in 'post-kala-azar leishmaniasis' (leishmanoid, PKDL, post-kala-azar dermal leishmaniasis), nodular, macular or maculopapular lesions may occur on body 1-2 y after treatment of visceral disease

Prototheca: non-tender, pyoderma-like or infiltrating lesions

Treatment:

***Simplexvirus*:**

Cold Sores:

Minor: aciclovir 5% cream every 4 h while awake for 5 d, commencing at first signs of onset

Severe Primary or Recurrent or Complicated by Erythema Multiforme: famciclovir 125 mg orally 12 hourly for 5 d, valaciclovir 500 mg orally 12 hourly for 5 d, aciclovir 10 mg/kg to 400 mg orally 8 hourly for 5 d (preferred for children and pregnant)

Unable to Swallow: aciclovir 5 mg/kg i.v. 8 hourly for 5 d (adjust dose for renal function)

Frequent Disabling Recurrences, Frequent Recurrences Complicated by Erythema Multiforme, HIV-infected Patients with Chronic Lesions: valaciclovir 500 mg orally daily for up to 6 mo, aciclovir 5 mg/kg to 200 mg orally 12 hourly for up to 6 mo (preferred for children or pregnant)

Mucocutaneous *simplexvirus* in Immunocompromised: aciclovir (preferred in children and pregnant) 5 mg/kg i.v. (adjust dose for renal function) or 10 mg/kg to 400 mg orally 5 times daily 8 hourly for 7-10 d, valaciclovir 1 g orally 12 hourly for 7 d, famciclovir 250 mg orally 8 hourly for 7 d (500 mg orally 8 hourly for 10 d in immunocompromised)

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

Eczema Herpeticum: valaciclovir 500 mg orally 12 hourly until healed, famciclovir 250 mg orally 12 hourly until healed, aciclovir 5 mg/kg to 200 mg orally 5 times daily until healed

More Severe: aciclovir 5 mg/kg i.v. 8 hourly then as above

Orf: typically resolve spontaneously in 4-6 w; liquid nitrogen cryosurgery speeds resolution; razor blade shaving effective when lesions persist; 35% idoxuridine in dimethylsulfoxide on eyelids; 0.5% idoxuridine ointment in conjunctival infection

Other Viruses: non-specific

***Streptococcus pyogenes*, *Neisseria*:** penicillin, erythromycin

***Francisella tularensis*:** streptomycin

Other Gram Negative Bacilli: gentamicin

***Staphylococcus aureus*:** penicillin (if isolate susceptible), penicillinase-resistant penicillin, clindamycin, erythromycin, cephalosporin, tetracycline

Corynebacterium jeikeium: vancomycin

***Listeria monocytogenes*:** erythromycin 500 mg orally 6 hourly (child: 30 mg/kg daily in 4 divided doses) for 5 d

Clostridium botulinum: penicillin + antitoxin

***Rickettsia*:** tetracycline, chloramphenicol

***Candida*:** topical nystatin, clotrimazole, miconazole ± oral ketoconazole, fluconazole

***Ajellomyces dermatitidis*:** amphotericin B

***Drechslera*:** excision biopsy + amphotericin B

***Rhizopus*:** debridement + topical povidone iodine

***Aspergillus*:** high dose amphotericin B + flucytosine

Leishmania:

***Leishmania braziliensis* and *Leishmania mexicana*:** sodium stibogluconate 200 mg Sb/kg/d i.m. or i.v. daily for 20 d or until decided improvement, amphotericin B 0.25-1 mg/kg daily on alternate days i.v. for up to 8 w, metronidazole 200 mg (child: 7.5 mg/kg) orally 3 times daily for 10 d, ketoconazole, pentamidine isethionate, allopurinol; intranodular injection of recombinant interleukin 2; lesions due to *Leishmania mexicana mexicana, Leishmania amazonensis* and *Leishmania pifanoi* may be incurable

***Leishmania aethiopica*:** sodium stibogluconate 18-20 mg/kg i.v. twice daily for 30 d

***Leishmania tropica*:** sodium stibogluconate 10mg/kg daily i.m. or i.v. for 6 d; paromomycin 15% or methylbenzethonium 12% ointment applied twice daily; oral fluconazole 200 mg daily for 6 w

Prophylaxis (Cutaneous Leishmaniasis): 100% successful frozen vaccine trialled in Brazil

Warts (Verruca): common (verruca vulgaris: solid, circumscribed, elevated tumour with multiple horny projections), flat (verruca plana juvenilis: smooth, slightly raised, occurring in large numbers), plantar (verruca plantaris: conical, bulging from skin surface on sole of foot), venereal (condyloma acunimatum: clusters of soft, fleshy lesions), laryngeal papillomas; 0.6% of new episodes of illness in UK; 0.4% of ambulatory care visits in USA

Agent: *human papillomavirus*

Diagnosis: cytology; cytoplasmic fluorescence (smooth muscle)

Treatment:

Oral, Cervical, Rectal, Anorectal, Pregnancy: cryotherapy, electrosurgery, surgical removal, bichloroacetic acid, trichloroacetic acid, intralesional interferon-α

Urethral: 5-fluorouracil, thiotepa

Others: podophyllin, podofilox, imiquimod, cryosurgery, surgical removal, duct tape occlusion

Pinta (Carate, Azul, Boussarole, Mepeines, Lota, Mal De Los Pintos, Mal Del Pinto, Painted Sickness, Tian): acute and chronic; transmission by direct contact

Agent: '*Treponema carateum*' (invalid name)

Diagnosis: first stage (primary pinta) manifested as small erythematous scaly papule (chancre of pinta) at site of inoculation 3-60 d after infection; satellite lesions may appear and coalescence occur; second stage (secondary pinta) manifested by generalised papular eruption appearing 5-12 mo after primary papule; papules (pintids) may show striking colours (pink, red, yellow, brown, blue, violet, black); third stage (late pinta, tertiary pinta) manifested principally by depigmentation (chromia, vitiligo) of lesions, which ultimately become white and atrophy, resulting in disfigurement; may be latent stage; serology

Treatment: penicillin

Acne Vulgaris (Pimples): 0.7% of ambulatory care visits in USA

Agents: primarily physiological, but *Propionibacterium acnes* may considerably aggravate symptoms by stimulating inflammation, and *Staphylococcus aureus* infection may supervene

Diagnosis: pus swab (restricted to *Staphylococcus aureus* superinfection; despite its undoubted role, (anaerobic) culture for *Propionibacterium acnes* is pointless; other organisms that may be isolated are also irrelevant

Treatment:

Mild: face washes with 2% w/w Triclosan liquid soap; adapalene 0.1% or water-based benzoyl peroxide 2.5 % increasing to 10% or isotretinoin 0.05% or tretinoin 0.025% increasing to 0.1% topically at night

Moderate Not Responding to Measures Above: clindamycin 1% lotion or erythromycin 2% gel topically in the morning; if insufficient response, replace with doxycycline 50-100 mg orally daily (not pregnant or breastfeeding), minocycline 50-100 mg orally daily (not pregnant or breastfeeding) or erythromycin 250-500 mg orally 12 hourly reducing to 250-500 mg daily

Severe or Cystic: refer to dermatologist

Pyoderma (Purulent Dermatitis), Boil, Carbuncle, Furunculosis, Pustulosis, Stye, Sycosis Barbae, Folliculitis (Bockhardt Folliculitis, Bockhardt Impetigo, Superficial Pustulosis Perifolliculitis), Hiradenitis: boil = furuncle = nodule found in cutaneous and subcutaneous tissues, usually around a hair follicle, characterised by inflammation and having a central core; carbuncle = network of furuncles connected by sinus tracts;

folliculitis = papular or pustular inflammation of hair follicles; sycosis barbae = multiple folliculitis of the bearded area of the face; hiradenitis = disease of sweat glands; 0.7% of new episodes of illness in UK; exclude diabetes if recurrent; friction, perspiration, obesity, blood dyscrasias, corticosteroid therapy and defective neutrophils other predisposing factors; also eosinophilic folliculitis in HIV-infected patients on triple therapy

Agents: *Staphylococcus aureus*, occasionally in association with *Streptococcus pyogenes*; *Aeromonas hydrophila; Pseudomonas aeruginosa* (pyoderma; folliculitis associated with spas and whirlpools), *Mycobacterium fortuitum* (furunculosis associated with nail salon footbaths); folliculitis also *Malassezia*, dermatophytes and *simplexvirus*

Diagnosis: culture of swab of lesions

***Pseudomonas aeruginosa*:**

Pyoderma: pre-existing lesion (exfoliative skin disease, venous stasis ulcer, eczema) colonised and subsequently invaded (especially when treated with occlusive dressings); characteristic moth-eaten appearance and erythematous border; acute and invasive or chronic indolent (slowly progressive, burrowing inflammation, forming coalescent papulopustular lesions covered with malodorous crust); swab culture, clinical differentiation of true infection from colonisation

Folliculitis: discrete, maculopapular lesions few mm in diameter, developing vesicle or pustule on apex, on trunk or proximal extremities, predominantly axillae and pelvis

Treatment:

***Staphylococcus aureus*:** if extensive lesions, cellulitis or systemic symptoms, di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly for 5 d

Penicillin Hypersensitive (Not Immediate): cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 5 d

Immediate Penicillin Hypersensitivity: clindamycin 10 mg/kg to 450 mg orally 8 hourly for 5 d

Remote Areas: di/flucloxacillin orally 12 hourly for 5-10 d + probenecid orally 12 hourly for 5-10 d; di/flucloxacillin orally 6 hourly for 5-10 d; erythromycin orally 12 hourly for 5-10 days; roxithromycin orally daily for 5-10 d

***Aeromonas hydrophila*:** gentamicin, ciprofloxacin

***Pseudomonas aeruginosa*:**

Pyoderma: long-term oral ciprofloxacin

Folliculitis: usually self-limiting; topical 0.1% polymyxin B or washing with antibacterial soap followed by alcohol-based drying solution can be used if necessary

Mycobacterium fortuitum: 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

Prophylaxis (Recurrent *Staphylococcus aureus* Infections): sorbolene cream with glycerol 10% before and after showering; mupirocin 2% nasal ointment applied to nostrils 3 times daily for 5 d + triclosan 1% wash or chlorhexidine 2% wash daily as a shampoo and for showering, and wash clothes, towels and sheets in hot water on 2 separate occasions

Continued Recurrence Despite Above Measures: + rifampicin 7.5 mg/kg to 300 mg orally 12 hourly for 7 d + di/flucloxacillin 12.5 mg/kg to 250 mg orally 6 hourly for 7 d or cotrimoxazole 4 + 20 mg/kg to 160 + 800 mg orally 12 hourly for 7 d or fusidate sodium 12 mg/kg to 500 mg orally 12 hourly for 7 d or fusidic acid suspension 18 mg/kg to 750 mg orally 12 hourly for 7 d

IMPETIGO: bullous (Cortell pyosis, impetigo bullosa, impetigo contagiosa bullosa, impetigo neonatorum, impetigo staphylogenes, Manson pyosis, pemphigus contagiosus, pemphigus neonatorum, pyoderma superficialis, staphylococcal impetigo) and non-bullous (Fox impetigo, impetiginous dermatitis, impetigo contagiosum, impetigo vulgaris, school sores) forms; 0.4% of new episodes of illness in UK; especially in children; transmission by contact with lesions, inoculation with person's own indigenous flora; incubation period 1-5 d

Agents: *Staphylococcus aureus* (both forms), *Streptococcus pyogenes* (non-bullous; streptococcal pyoderma—especially US; glomerulonephritis may follow within 8 w), Group C *Streptococcus*

Diagnosis: swab culture

Bullous: superficial skin blebs (bullae), which usually rupture and form yellowish crusts; may spread by autoinoculation, with appearance of satellite lesions in the vicinity; in neonates and young children

Non-bullous: vesicles which become pustular and form honey-coloured crusts, each lesion being surrounded by an erythematous zone

Treatment: remove crusts 8 hourly with saline or soap and water or aluminium acetate solution or potassium permanganate solution

***Streptococcus pyogenes* Primary Pathogen:** phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly for 5 d, benzathine penicillin 30-45 mg/kg to 900 mg i.m. as single dose

Penicillin Hypersensitive: roxithromycin 300 mg orally daily (child: 4 mg/kg to 150 mg orally 12 hourly) for 10 d

Staphylococcus aureus: mupirocin 2% topically 8 hourly for 7 d

Severe Cases or if Cellulitis Present or if Recurrent: di(flu)cloxacillin 12.5 mg/kg to 250 mg orally 6 hourly for 10 d; cephalexin 12.5-25 mg/kg to maximum 250 mg orally 6 hourly for 10 d if penicillin hypersensitive (not immediate); roxithromycin 300 mg orally daily (child: 4 mg/kg to 150 mg orally 12 hourly) for 10 d if immediate penicillin hypersensitivity

Prevention and Control: hygiene; in recurrent or resistant cases, nasal and/or perineal swabs of whole family and close contacts and treatment if positive (see **PROPHYLAXIS (RECURRENT *STAPHYLOCOCCUS AUREUS* INFECTIONS)** above

TOXIC EPIDERMAL NEUROLYSIS (ALLERGIC BULLOUS DERMATOSIS, DERMATITIS ERYSIPELATOSA, DERMATITIS EXFOLIATIVA INFANTUM, DERMATITIS EXFOLIATIVA NEONATORUM, EPIDERMIOLYSIS ACUTA TOXICA, EPIDERMIOLYSIS COMBUSTIFORMIS ACUTA, KERATOLYSIS NEONATORUM, LYELL DISEASE, LYELL SYNDROME, RITTER DERMATITIS, RITTER DISEASE, RITTER VON RITTERSHAIN DISEASE)

Agents: *Staphylococcus aureus* (reaction to toxin, exfoliatin, produced by certain strains), certain other microorganisms, certain pharmaceuticals (including numerous antibiotics)

Diagnosis: erythema, formation of bullae, separation of epidermis, continued desquamation; swab culture

Treatment: penicillinase-resistant penicillin, erythromycin, clindamycin; healing is usually complete in 2 w with adequate treatment

ERYSIPELAS (IGNIS SACER, ST ANTHONY'S FIRE, ST FRANCIS' FIRE): acute disease of skin and subcutaneous tissues; predisposing factors newborn and elderly, nephrotic syndrome, preexisting lymphatic obstruction or edema, prior episode of erysipelas, any break in skin; 0.01% of new episodes of illness in UK; considerable toxic component

Agents: *Streptococcus pyogenes*; similar condition due to *Yersinia enterocolitica*

Diagnosis: raised, edematous, red area of inflammation that is well demarcated, especially when it affects a part of the body where the skin is taut (eg., the forehead); culture of skin blebs swab (also throat swab and wound swab); blood cultures; serology (ASOT, anti-DNAse B); neutrophilia in most cases

Differential Diagnosis: early herpes zoster, contact dermatitis, giant urticaria, inflammatory carcinoma

Treatment:

***Streptococcus pyogenes*:** possibility of glomerulonephritis developing with toxigenic strains should be borne in mind

Severe: benzylpenicillin 30 mg/kg to 600 mg i.v. 4 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly, cephazolin 50 mg/kg/d to 2 g i.v 8 hourly

Immediate Penicillin Hypersensitivity: clindamycin 10 mg/kg to 450 mg i.v. or orally 8 hourly, lincomycin 25 mg/kg to 600 mg i.v. 8 hourly, vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. slowly 12 hourly (monitor blood levels and adjust dose accordingly)

Less Severe: procaine penicillin 50 mg/kg to 1.5 g i.m. daily for at least 3 d, phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly for 10 d

Penicillin Hypersensitive (Not Immediate): cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 7-10 d

Immediate Penicillin Hypersensitivity: clindamycin 10 mg/kg to 450 mg orally 8 hourly for 7-10 d

***Yersinia enterocolitica*:** cotrimoxazole

ERYSIPELOID (FISH HANDLER'S DISEASE; DIAMONDBACK, DIAMOND SKIN INFECTION, SWINE ERYSIPELAS IN ANIMALS): cutaneous erysipeloid (erythema migrans, erythema serpens, Rosenbach disease, Rosenbach erysipeloid, Rosenbach rouget) and disseminated erysipeloid (Klauder disease; rare)

Agent: *Erysipelothrix rhusiopathiae*

Diagnosis: contact with pigs or fish; butcher, cook or fish handler; culture of swab of material under skin over inflammatory swelling

Cutaneous Erysipeloid: most frequently on skin of hand or forearm; pruritic, purplish-red patch that is slightly indurated and has a slightly raised margin, which spreads centrifugally while centre heals; recovery usually spontaneous after 2-3 w

Disseminated Erysipeloid: diffuse generalised skin lesions with fever and generalised lymphadenopathy

Treatment: penicillin, erythromycin

ERYTHRASMA

Agent: *Corynebacterium minutissimum*

Diagnosis: pink to brown irregular patches with fine creasing; coral pink fluorescence of lesion and scrapings under Wood's light; oil immersion microscopy of skin scraping (diphtheroids seen)

Treatment: erythromycin 1 g/d for 5-7 d

Dermatophilosis (Contagious Dermatitis, Epidemic Eczema, Sporotrichosis; Lumpy Wool in Sheep): common in cattle and, especially, sheep; rare in man

Agent: *Dermatophilus congolensis*

Diagnosis: multiple painless pustules on the dorsal surface of the hands 2-7 d after exposure to cattle, sheep or goats; Giemsa stain and culture of scabs and exudates

Treatment: penicillin + streptomycin

Cutaneous Anthrax (Malignant Carbuncle, Malignant Pustule): most common form of anthrax (> 95%); acquired from handling contaminated hides, carcasses, wool, etc; case-fatality rate 20% without antibiotic treatment, < 1% with antibiotics

Agent: *Bacillus anthracis*

Diagnosis: incubation period 1-6 d; pruritus at site of inoculation, followed by small, painless but itchy raised bump or papule, resembling insect bite, enlarging into 1-3 cm vesicles within 1-2 d and rupturing, draining serosanguineous fluid and leaving a painless depressed eschar 1-3 cm diameter with a characteristic black necrotic area in the centre and, sometimes, satellite vesicles, with edema out of proportion to size of lesion and regional lymphadenopathy in many cases; > 90% of lesions on exposed face, neck, arms and hands; occasionally, extensive local involvement, with severe edema, formation of bullae and septicemia (septicaemic cutaneous anthrax, malignant anthrax, malignant oedema); contact with cattle, sheep, pigs, hides; Gram stain (Gram positive rods and few neutrophils) and culture of vesicle fluid or from under edge of eschar; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test

Treatment: ciprofloxacin 15 mg/kg to 500 mg orally twice a day or doxycycline 2.5 mg/kg to 100 mg orally twice a day (not < 8 y) till clinical improvement then amoxicillin 15 mg/kg to 500 mg orally 3 times a day for total 60 d

Severe or Associated with Systemic Symptoms: ciprofloxacin 400 mg i.v. every 12 h or doxycycline 100 mg i.v. every 12 h + rifampicin, vancomycin, clindamycin, penicillin, chloramphenicol, imipenem, amoxy/ampicillin or clarithromycin

Prophylaxis (Post-exposure): oral doxycycline or ciprofloxacin as above; consider 3 doses of anthrax vaccine 0, 2 and 4 w after exposure

Cutaneous Diphtheria: disease of the skin that, on rare occasions, has been associated with diphtheric throat infections; more commonly, especially in tropics, disease is result of infection of open sores, wounds and eczematous skin lesions; cases in Aborigines in Central Australia

Agent: *Corynebacterium diphtheriae*

Diagnosis: primary cutaneous diphtheria may occur as a single or several pustules, usually on lower extremity, progressing to a punched-out ulcer covered by grey-brown membrane; often fatal myocarditis or diphtheric polyneuritis (post-diphtheric paralysis) may occur; Albert's or Neisser stain and culture of swab of lesion

Treatment: isolation and bed rest + antitoxin 10,000-100,000 U depending on severity; always precede by test for allergy to horse serum

Carriers: erythromycin 500 mg orally 6 hourly (child: 30-40 mg/kg daily orally in 3 divided doses), procaine penicillin 600,000 U i.m. 12 hourly for 10 d (child: 25,000-50,000 U/kg i.m. daily in 2 divided doses)

Cutaneous and Mucocutaneous bartonellosis (Bouton Des Andes, Peruvian Wart, Verruga Andicola, Verruga Peruana): appears weeks or months after termination of systemic bartonellosis or, on rare occasions, without primary history of systemic illness

Agent: *Bartonella bacilliformis*

Diagnosis: pleomorphic eruption of hemangiomatous papules and nodules that gradually assume aspect of warts, usually localised in skin but sometimes in subcutaneous tissue, mucous membranes, muscles, bones or viscera; organisms seen in endothelial cells in stained smears of material from granulomatous skin lesions; blood cultures

Treatment: tetracycline

Acute Skin Ulcers

Agents: *Francisella tularensis, Chromobacterium violaceum* (in 11% of infections), *Flavobacterium meningosepticum* (waterborne), *Pseudomonas paucimobilis*

Diagnosis: culture of lesion swab, lymph node aspirate, blood

Treatment:

***Francisella tularensis*:** streptomycin, tetracycline

***Chromobacterium violaceum*:** chloramphenicol

***Flavobacterium meningosepticum*:** clindamycin

***Pseudomonas paucimobilis*:** ciprofloxacin

Chronic Skin Ulcers

Agents: *Arcanobacterium haemolyticum, Corynebacterium bovis, Mycobacterium marinum* (swimming pool granuloma, swimming pool granuloma disease), *Mycobacterium ulcerans* (Bairnsdale ulcer, Buruli ulcer, Searl ulcer; third most prevalent

mycobacterial disease), *Mycobacterium chelonae,* other mycobacteria; may be complicated by superinfection with *Streptococcus pyogenes* and *Staphylococcus aureus*

Diagnosis: Gram stain and Ziehl-Neelsen stain and culture at 30-34°C and 37°C of ulcer swab or biopsy

***Mycobacterium marinum*:** chronic granulomatous nodules or cutaneous or subcutaneous ulcers

Mycobacterium ulcerans: painless, firm nodule with erythema and induration progressing to painless ulcer with undermined edges and necrotic slough containing extracellular acid-fast bacilli

Differential Diagnosis: blastomycosis (pulmonary lesions commonly present; biopsy and culture), chromoblastomycosis (biopsy and culture), foreign body granuloma (history of trauma may be available; absence of significant bacteria on stain and culture), inoculation tuberculosis (rare; occupational history; biopsy and culture of lesion), sporotrichosis (history of work or hobby; biopsy and culture), nocardial infection (acid fast stain and culture), nodular fasciitis, injection abscess and panniculitis (biopsy with special stains)

Treatment:

***Arcanobacterium haemolyticum, Corynebacterium bovis*:** erythromycin + rifampicin

***Mycobacterium marinum*:** may resolve spontaneously or on curettage; clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly, cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly, doxycycline 2.5 mg/kg to 100 mg orally (not < 8 y) 12 hourly

***Mycobacterium ulcerans*:** wide excision and skin grafting, local heat + rifampicin and amikacin for 8 w

Mycobacterium chelonae: clarithromycin 500 mg twice a day

Other Mycobacteria: excision; streptomycin + dapsone ± ethambutol

Tropical Ulcer (Aden Ulcer, Cochin Sore, Malabar Ulcer, Mozambique Ulcer, Nagana Sore, Necrotising Ulcer of the Skin Surface, Phagedana Tropica, Tropical Phagedaena, Tropical Phagedena, Tropical Phagedenic Ulcer, Tropical Sloughing Phagedena, Ulcus Tropicum, Yemen Ulcer): causes 2% of fever in returned travellers to Australia

Agents: believed to be due to a mixed infected with *Treponema vincentii* and 'fusiform' bacteria such as *Leptotrichia buccalis*

Diagnosis: chronic, usually solitary, ulcer occurring most commonly in tropical areas and characterised by sloughing of tissue; Gram stain or simple stain of swab of lesion

Treatment: metronidazole

Ischemic, Varicose and Decubitus Skin Ulcers

Agents: colonised by various bacteria

Diagnosis: clinical; culture of deep tissue biopsy; computed tomography, magnetic resonance imaging, bone biopsy and histopathological evaluation to detect osteomyelitis

Treatment: antibiotics are not required unless cellulitis or osteomyelitis is present or the patient is diabetic (treat as for **Ulcers in Diabetics**); extirpation by physical means or enzymes or maggot debridement may sometimes be indicated; bismuth formic iodide powder or povidone iodine gauze pads may sometimes be useful in controlling excessive colonisation; treatment should be aimed at correction or prevention of the precipitating cause

Skin Ulcers in Diabetics (Foot and Leg Sores)

Agents: coliforms, *Proteus*, anaerobes, *Staphylococcus, Streptococcus*, numerous others; all isolates may be significant except coagulase negative staphylococci, *Micrococcus*, skin flora coryneforms

Diagnosis: Gram stain of direct smear, culture of swab in Stuart's transport medium of sore (deeper specimens give no greater information)

Treatment: should always be regarded as serious and treated vigorously; surgical or maggot debridement if necessary; consider underlying osteomyelitis

Severe: ticarcillin-clavulanate 3/0.1 g i.v. 6 hourly, piperacillin-tazobactam 4/0.5 g i.v. 8 hourly, meropenem 500 mg i.v. 8 hourly; recombinant granulocyte colony stimulating factor reduces amputation rate in limb-threatening foot infections

Penicillin Hypersensitive: ciprofloxacin 400 mg i.v. or 750 mg orally 12 hourly + clindamycin 900 mg i.v. 8 hourly by slow infusion or lincomycin 900 mg i.v. 8 hourly by slow infusion

Less Severe: metronidazole 400 mg orally 12 hourly + cephalexin 500 mg orally 6 hourly; amoxycillin-clavulanate 875/125 mg orally 12 hourly for at least 5 d

Penicillin Hypersensitive: ciprofloxacin 500 mg orally 12 hourly + clindamycin 600 mg orally 8 hourly for at least 5 d

Trichosis Axillaris (Lepothrix, Trichomycosis Axillaris): superficial disease of axillary or pubic hairs

Agent: '*Corynebacterium tenuis'* (invalid name)

Diagnosis: adherent yellow, red or black nodules on hair shaft; microscopy of hair

Treatment: shaving; sulphur ointment

Black Piedra: mainly tropical

Agent: *Piedraia hortae*
Diagnosis: micro and culture of nodules on hair shafts
Treatment: shaving; sulphur ointment

WHITE PIEDRA

Agent: *Trichosporon cutaneum*
Diagnosis: microscopy and culture of infected hairs
Treatment: shaving; sulphur ointment

CHROMOBLASTOMYCOSIS (VERRUCOUS DERMATITIS, CHROMOMYCOSIS, MOSSY FOOT)

Agents: *Cladophialophora carrionii* (in Australia, S.Africa, Venezuela), *Fonsecaea compacta* and *Fonsecaea pedrosoi* (in Far East), *Phialophora verrucosa*, *Rhinocladiella*
Diagnosis: slow development of warty skin nodules, with subsequent development of elephantiasis when lymphatics involved in chronic inflammation, accompanied by fibrotic change in deeper tissues; visualisation of fungus in wet preparations; fungal culture of crusts, pus, biopsy; complement fixation test
Treatment: surgical excision; flucytosine 25 mg/kg orally 6 hourly (< 50 kg: 1.5-4.5 g/m^2 orally daily) + thiabendazole 25 mg/kg orally daily or amphotericin B under expert supervision; ketoconazole 200-400 mg orally (child < 20 kg: 50 mg; 20-40 kg: 100 mg; > 40 kg: 200 mg) daily ± flucytosine 25 mg/kg orally 6 hourly (< 50 kg: 1.5-4.5 g/m^2 orally daily); itraconazole 200-400 mg orally (child: 3.5 mg/kg) once daily (not in pregnancy)

PHAEOHYPHOMYCOSIS

Agents: *Alternaria alternata*, *Cochliobolus hawaiiensis, Cladophialophora bantiana, Curvularia geniculata, Exophiala jeanselmei, Exophiala moniliae, Exophiala pisciphila, Bipolaris spicifera, Exserohilum rostratum, Phaeoannellomyces elegans, Lecythophora hoffmannii, Phaeoacremonium parasiticum* (may disseminate to contiguous joint), *Pleurostomophora repens, Pleurostomophora richardsiae, Exophiala spinifera, Phialophora verrucosa, Phoma, Pleurophoma, Exophiala dermatitidis*
Diagnosis: biopsy and culture of lesions
Treatment: surgical excision; amphotericin B, topical miconazole, topical dry heat

CUTANEOUS CRYPTOCOCCOSIS: found in ≈ 10% of cases, usually in disseminated cases; rarely primary; cystic or firm subcutaneous swellings which ulcerate, crusted granulomas, plaques or nodules, ulcers; mucosal lesions in ≈ 3%
Agent: *Cryptococcus neoformans*
Diagnosis: biopsy and culture of lesions
Treatment:

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

CUTANEOUS CANDIDIASIS: intertriginous, thrush, perleche on angles of lips, paronychia, 5% of tinea pedis; 0.2% of ambulatory care visits in USA
Agent: *Candida albicans*, other *Candida* species
Diagnosis: micro (small oval budding yeast cells, sometimes with pseudohyphae, which do not take up Quink ink) and culture of swab of scrapings
Treatment: keep affected area as clean and dry as possible; nystatin 100,000 U/g, miconazole 2%, clotrimazole 1% or econazole 1% applied topically 8-12 hourly, continuing for 2 w after symptoms resolve

CUTANEOUS BLASTOMYCOSIS

Agent: *Ajellomyces dermatitidis*
Diagnosis: visualisation of buds in wet preparations, confirmed by culture
Treatment: ketoconazole 200-400 mg orally daily for up to 1 y, hydroxystilbamidine isethionate 225-250 mg (child: 3-4.5 mg/kg) i.v. daily to total dose of 8 g, itraconazole

CUTANEOUS HISTOPLASMOSIS

Agent: *Histoplasma capsulatum*
Diagnosis: visualisation of fungi in pus or skin biopsy, confirmed by culture; may become disseminated in patients infected with human immunodeficiency virus
Treatment: surgery

TINEA AND RINGWORM: transmission from human and animal lesions, contaminated objects; 0.8% of new episodes of illness in UK; 0.3% of ambulatory care visits in USA; common worldwide
Agents: *Epidermophyton floccosum* (anthropophilic; groin and other intertrigo infections, especially under breasts, less commonly elsewhere on body, including feet and nails), *Microsporum audounii* (epidemic scalp infections, tinea corporis), *Microsporum canis* (zoophilic; ringworm and nonepidemic scalp infections; 75% of tinea capitis in Queensland; reservoir cats

and dogs), *Microsporum gypseum* (geophilic; ringworm; 11% of tinea capitis in Queensland; severe infection with kerion), *Athroderma cajetani* (foot), *Microsporum ferrugineum* (ringworm of scalp and glabrous skin; Africa, India, China, Japan), *Athroderma fulvum* (sporadic tinea corporis, tinea capitis, tinea barbae), *Athroderma obtusum* (body), *Scedosporium* (rare onychomycosis), *Trichophyton mentagrophytes var granulosum* (zoophilic; ringworm on arms, legs, torso, scalp and beard infections), *Trichophyton interdigitale* (anthropophilic; tinea pedis, tinea mannus, tinea cruris, tinea unguium), *Trichophyton erinacei* (scalp, body), *Trichophyton rubrum* (anthropophilic; tinea pedis, tinea cruris, lesions and rashes elsewhere on body, including beard, arms, legs, torso, hands, nails), *Trichophyton schoenleinii* (tinea favosa of scalp, torso), *Trichophyton tonsurans* (epidemic scalp infections, tinea corporis, sycosis, onychomycosis; common in Aborigines; 11% of tinea capitis in Queensland, 96% in USA), *Trichophyton verrucosum* (nonepidemic scalp infections, tinea barbae, ringworm), *Trichophyton violaceum* (tinea favosa of scalp, torso, onychomycosis), *Trichophyton concentricum* (body), *Trichophyton equinum* (from horses), *Trichophyton soudanese* (tinea capitis, tinea corporis), *Trichophyton terrestre* (all sites except scalp, face), *Curvularia lunata* (rare onychomycosis)

Diagnosis: Wood's UV light of infected skin; micro of KOH-Parker Quink preparation (long, branching, hyaline, septate strands of hyphae) of skin, histopathologic sections of biopsy material stained with periodic acid-Schiff, culture (dermatophyte test medium most sensitive) of appropriate specimen:

Skin Lesions: scraping from periphery

Nail Infections: nail clippings and scrapings of inner margin of infected area, subungual debris

Scalp: plucked hairs (especially Wood's light positive ones), scraping from lesion

Tinea Pedis with Vesicular Eruption: domes of vesicles snipped off, swab of fluid and scraping from base of vesicle (note that tinea pedis frequently–especially under occlusion–becomes secondarily infected with Gram negative bacteria (particularly *Pseudomonas aeruginosa*), which change the normal dry, scaling condition into a painful, hyperkeratotic or erosive process with exudation and intense inflammation; under such conditions, dermatophytes will be demonstrated in only about 25% of cases)

Treatment:

Tinea Corporis, Pedis and Cruris: bifonazole 1% topically once daily, terbinafine 1% topically once or twice daily, clotrimazole 1% topically 2 or 3 times daily, econazole 1% topically 2 or 3 times daily, ketoconazole 2% topically twice daily, miconazole 2% topically twice daily, continuing for 2 w after symptoms resolve

Unresponsive Cases: terbinafine (< 20 kg: 62.5 mg; 20-40 kg: 125 mg; > 40 kg: 250 mg) orally once daily for at least 2 w, griseofulvin fine particle 10 mg/kg to 500 mg or ultrafine particle 5.5 mg/kg to 330 mg (not < 2 y) orally once daily for at least 4 w

Web Infections Due to *Pseudomonas Aeruginosa*: cleaning, debriding infected skin, avoiding wetness, dilute acetic acid

Tinea Capitis: terbinafine (< 20 kg: 62.5 mg; 20-40 kg: 125 mg; > 40 kg: 250 mg) orally daily for 4 w, griseofulvin microsize (fine particle) 10 mg/kg to 500 mg orally once daily with milk for 4-8 w, griseofulvin ultramicrosize (ultrafine particle) 5.5 mg/kg to 330 mg orally daily crushed and taken with chocolate chip ice cream for 4-8 w (not < 2 y); + 1% selenium sulphide or 2% ketoconazole shampoo

Tinea Unguium (Onychomycosis): terbinafine (< 20 kg: 62.5 mg; 20-40 kg: 125 mg; > 40 kg: 250 mg) orally daily for 6 w (finger nails) or 12 weeks (toe nails), amorolfine nail lacquer applied to affected nail after filing down once or twice weekly for at least 6 months, griseofulvin or ketoconazole as for **Tinea Capitis**

Prevention and Control: hygiene

TINEA VERSICOLOR (CHROMOPHYTOSIS, DERMATOMYSOSIS, FURFURACEA, PITYRIASIS, PITYRIASIS VERSICOLOR, PITYRIASIS VERSICOLOR TROPICA, TINEA FLAVA)

Agent: *Malassezia furfur*

Diagnosis: micro of KOH-Parker Quink preparation of skin scrapings from macules especially those fluorescing under Wood's light (round, budding yeast cells and occasionally branched, truncate hyphae of variable length)

Treatment: econazole 1% solution topically to wet skin and left overnight for 3 nights; ketoconazole 2% shampoo topically daily for 10 minutes and washed off, for 10 d; selenium sulphide 2.5% suspension topically to wet skin for at least 10 min or overnight, for 1-2 w, topical sodium thiosulphate 25% (wash off after 10 min) for 2-4 w

Unresponsive: ketoconazole 200 mg orally daily for 10 d, itraconazole 200 mg orally daily for 5 d

TINEA NIGRA

Agent: *Hortaea werneckii*

Diagnosis: micro (dematiaceous tortuous hyphae with abundant branching and elongated yeast cells) and culture of skin scrapings or biopsy

Treatment: amphotericin B

CUTANEOUS AMOEBIASIS (AMOEBIASIS CUTIS, AMOEBIC SKIN ULCERATION): usually arises as extension of intestinal amoebiasis, hepatic amoebiasis or amoebic lung abscess but on occasion results from primary infection; 'genital amoebiasis' may lead to destruction of external genitalia

Agent: *Entamoeba histolytica*
Diagnosis: painful, rapidly spreading edematous ulceration of skin; usually fever and leucocytosis; biopsy
Treatment: metronidazole

CUTANEOUS LARVA MIGRANS (CREEPING ERUPTION, DERMATITIS LINEARIS MIGRANS, PLUMBER'S ITCH): humid tropical areas; parasites migrate in dermis
Agents: mainly *Ancylostoma braziliense* (hookworm larvae of dogs and cats); also *Ancylostoma caninum, Ancyclostoma ceylanicum, Ancyclostoma duodenale, Necator americanus, Strongyloides stercoralis* and nonhuman *Strongyloides* species, *Uncinaria stenocephala, Anatrichosoma haycocki* (very rare)
Diagnosis: multiple, subcutaneous, reddish-purple, pruritic, progressive, linear, papulovesicular lesions on sole of feet, with raised serpiginous lines developing; histology (may be local eosinophilic or round-cell infiltration); eosinophilia and anemia; neutrophilia in children
Treatment: usually self-limiting but treatment alleviates symptoms; individual larvae can be killed by spraying the tracks with ethyl chloride; ivermectin 200 μg/kg orally as single dose (not < 5 y), albendazole (≤ 10 kg: 200 mg; >10 kg: 400 mg) once daily for 3 d (not in pregnancy, lactation or < 6 mo)

SPIROMETROSIS (LARVAL DIPHYLLOBOTHRIASIS, SPARGANOSIS, SPARGANUM INFECTION)
Agent: *Spirometra* species; larvae migrate through subcutaneous tissue
Diagnosis: inflammation and edema of skin; migration around eye produces painful edematous conjunctivitis and lacrimation; histology
Treatment: as for **CUTANEOUS LARVA MIGRANS**

DRACUNCULIASIS (DRACONTIASIS, DRACUNCULOSIS, GUINEA WORM DISEASE, MEDINA INFECTION, MEDINA WORM INFECTION): 69% in Sudan, remainder in 12 other sub-Saharan African countries; incidence 96,000 in 1999; no deaths reported
Agent: *Dracunculus medinensis*
Diagnosis: incubation period (≈ 1 y) with no symptoms; urticaria, erythema, dyspnoea, vomiting, diarrhoea, intense pruritus, giddiness (great variability) prior to eruption of cutaneous blister which ruptures and discharges larvae on contact with water and may develop into ulcer; infection gives rise to cellulitis and abscesses, 40% of patients having severe disability lasting 43 d, while 0.5-1% of cases suffer permanent damage from joint infection; larvae in aspirate from fresh cutaneous ulcer; appearance of worm on emergence through skin; radiology may reveal calcified worms
Treatment: metronidazole 400 mg orally 8 hourly (child: 25 mg/kg daily in 3 divided doses) for 5 d, niridazole 12.5 mg/kg orally twice daily for 10 d, thiabendazole 25 mg/kg orally daily for 3 d
Prevention and Control: straining of water before drinking; step wells

GNATHOSTOMIASIS (GNATHOMIASIS, WANDERING SWELLING, YANGTSE OEDEMA)
Agent: *Gnathostoma* species
Diagnosis: local inflammation and transient granulomatous eosinophilic swelling; eosinophilia; history of travel to SE Asia or S America and ingestion of raw or inadequately cooked fish, poultry or pork
Treatment: removal of worm when appropriate

EXTERNAL HIRUDINASIS
Agents: leeches (*Haemadipsa* spp, *Phinobdella* spp)
Diagnosis: history; punctured skin heals slowly and there is often secondary pyogenic infection; multiple punctures have been fatal owing to loss of blood
Treatment: removal; treatment of secondary infection

TUNGIASIS (BURROWING FLEA INFESTATION, CHIGOE DISEASE, JIGGER DISEASE, NIGUA, SANDFLEA INFESTATION)
Agent: *Tunga penetrans;* pregnant female sandfleas burrow into epidermis, usually sole of foot or interdigital spaces
Diagnosis: intense pruritus and inflammation; may be severe secondary infection; identification of female removed from burrows in skin (usually of toes)
Treatment: removal

CUTANEOUS MYIASIS (DERMAL MYIASIS, DERMAMYIASIS, FURUNCULAR MYIASIS, MYIASIS DERMATOSA): infestation of skin or subcutaneous tissues by larvae of certain flies
Agents: *Cochliomyia hominivorax, Cochliomyia macellaria, Cordylobia anthropophaga, Dermatobia hominis, Phormia regina, Sarcophaga, Rhagoletis meigeni, Wohlfahrtia vigil*
Diagnosis: maculopapular, erythematous, intensely pruritic, becoming nodular boil-like furuncles, 1-2 cm diameter, volcano-like, episodically painful, centrally necrotic, with small amounts of bloody, serous or purulent drainage; recovery of larvae from lesions
Treatment: removal of larvae; debridement as necessary

CREEPING MYIASIS (MYIASIS LINEARIS): form of cutaneous myiasis caused by larvae of certain flies; migration of larvae may be either superficial or deeply penetrating; resembles cutaneous larva migrans

Agents: *Gasterophilus haemorrhoidalis*, *Gasterophilus intestinalis*, *Gasterophilus nasalis*, *Hypoderma bovis, Hypoderma lineatum*

Diagnosis: recovery of larvae

Treatment: removal of larvae

PEDICULOSIS AND PHTHRIASIS (CRAB-LOUSE INFESTATION, PHTHIROSIS): pediculosis and phthriasis pubis 5% of male sexually transmitted disease, 4% of female; 66% incidence in homosexuals

Agents: *Pediculus humanus capitis*, *Pediculus humanus corporis*, *Phthirus pubis*

Diagnosis:

***Pediculus humanus capitis*:** infestation of scalp and/or back of neck; severe pruritus, often pustular eczema; secondary infection resulting from scratching common

***Pediculus humanus corporis*:** infestation of body, usually parts in close contact with clothing; furuncles and erythematous maculopapular rash; often a pigmented thickening of skin with parallel scratch marks ('vagabond's disease'); secondary infection resulting from scratching common

***Phthirus pubis*:** infestation of pubic region; slight to severe pruritus; secondary infection resulting from scratching common; usually transmitted by sexual contact; may invade eyelids, causing disease resembling staphylococcal blepharitis; rare scalp infestation in children

Treatment:

Scalp and Body (Including Groin): malathion (maldison) 0.5% lotion (not < 6 mo), permethrin 1% crème rinse or pyrethrins 0.165% + piperonyl butoxide 1.65-4% in foam base to affected area, leave for 10 min, then wash off thoroughly, repeat in 1 w if necessary; lindane 1% shampoo applied for 4 minutes then washed off thoroughly (not pregnant or lactating or < 2 y); treat household child contacts and sexual contacts; wash underwear and bedclothes after treatment; use of fine tooth comb; shaving hair; hot air

Treatment Failure: 1% permethrin crème rinse + oral cotrimoxazole; ivermectin single dose

Eyelashes: occlusive ophthalmic ointment twice daily for 10 d

SCABIES (ITCH, ST MAIN EVIL, SARCOPTIC ITCH, SARCOPTIC MANGE): skin disease in which mites burrow under skin and feed on subcutaneous tissues; worldwide among poor and in geriatric homes; 2% of male sexually transmitted disease, 0.9% of female; 0.2% of new episodes of illness in UK

Agent: *Sarcoptes scabiei* (human strains cause scabies in humans; host-specific animal strains (dogs, horses, camels, etc) may produce a contact dermatitis)

Diagnosis: severe pruritus, usually vesiculation and papule formation; scratching often leads to secondary infection; under conditions such as immunosuppressive therapy, may become severe, mites multiplying in enormous numbers, with formation of extensive crusted lesions (crusted scabies, Norwegian scabies); mites obtained by scraping between fingers or toes or other infected areas with oil-moistened blade to microscope slide (scraping should be deep enough that flecks of blood appear in the oil)

Treatment:

< 6 mo: sulphur 10% (< 2 mo: 5%) in white soft paraffin daily for 2-3 d, crotamiton 10% cream daily for 2-3 d

Others: permethrin 5% cream, applied to whole body including face and hair (avoid eyes and mucous membranes, hot baths or scrubbing before application), left overnight and washed off thoroughly (not < 6 mo; recommended in pregnancy and lactation); benzyl benzoate 25% emulsion (2 mo - 2 y: dilute 1:3; 2-12 y and sensitive adults: dilute 1:1) applied to whole body including face and hair (avoid eyes and mucous membranes, hot baths or scrubbing before application), washed off after 24h; repeat after 1 w

Crusted Scabies: as above + ivermectin 200 μg orally on days 1 and 8 (less severe), 1, 2 and 8 (moderate) or days 1, 2, 8, 9 and 15 (severe; + days 22 and 29 if extremely severe) (not pregnant, lactating, < 5 y); repeat topical treatment twice weekly for 2-6 w; sailcyclic acid 5-10% in sorbolene cream or lactic acid 5% + urea 10% in sorbolene cream daily after washing on days scabicide not applied

Resistant Scabies in HIV: ivermectin 200 μg/kg orally weekly until scrapings negative and no further clinical evidence of infestation

ACARINE DERMATITIS

Agents: *Dermanyssus gallinae*, *Ornithonyssus sylvarum, Pyemotes, Demodex folliculorum, Tryophagus longior, Tryophagus putrescentiae* (cheese itch, copra itch, grocer's itch), *Acarus siro, Glycyphagus domesticus* (grocer's itch)

Diagnosis: recovery of mite

***Dermanyssus gallinae*:** lesions resemble those of scabies

Ornithonyssus sylvarum: urticarial weals, papules and vesicles; scratching may lead to secondary infection

Demodex folliculorum: hair follicles and sebaceous glands; usually mild pruritus and fibrous tissue response; rarely, dry chronic erythema with burning irritation and scaling of epidermis

***Glycyphagus domesticus*:** temporary pruritus

Treatment: symptomatic

TROMBICULOSIS (CHIGGER INFESTATION, SCRUB ITCH, TROMBICULIASIS, TROMBIDIASIS, TROMBIDIOSIS)

Agents: *Leptotrrombidium akamushi*

Diagnosis: severe dermatitis; usually pustular lesion at point of entry and severe itching; may be allergic reactions; recovery of mite

Treatment: symptomatic

BEE STING: reactions, when occurring, usually anaphylactic; no consistent blood changes

HORNET STING: in cases of multiple stings, toxic muscle damage with myoglobinemia and myoglobinuria and increased serum alanine aminotransferase, serum aspartate aminotransferase, creatine phosphokinase and lactate hydrogenase may occur; nephrotoxic effects with developing renal failure may also occur

Agent: *Vespa affinis*

SCORPION STING: causes marked neutrophilia and, in young children, acute pancreatitis, acute hemolytic anemia and defibrination syndrome

WASP STING: reactions, when occurring, usually acute anaphylactic

SPIDER BITE: causes neutrophilia, acute hemolytic anemia with thrombocytopenia

DISSEMINATED RASH

Agents: syphilis, yaws (infectious; 2-3 mo)

Diagnosis: serology

Treatment: penicillin

ERYTHEMATOUS RASH

Agents: Kawasaki disease (primarily trunk), rubella (transient; conjunctivitis ±, pharyngitis ±, rhinitis ±, enanthem ±; incubation period 12-23 d; children, occasionally adults; spring), *Streptococcus pyogenes* (scarlet fever; caused by toxin; pharyngitis ++, conjunctivitis ±, rhinitis ±, enanthem absent), *Staphylococcus aureus* ('staphylococcal scalding'; diffuse or palmar erythroderma in all cases of toxic shock syndrome), *Pseudomonas aeruginosa* ('*Pseudomonas* hot foot syndrome'; exquisitely tender erythematous plantar nodules traced to wading pool), Marburg virus disease (transient, shoulders and arms), enteroviruses; also niacin associated illness

Diagnosis: clinical; hemagglutination inhibition, complement fixation test; culture of nose swab, throat swab, lesions

Treatment:

Viruses: non-specific

Scarlet Fever: penicillin, erythromycin

***Staphylococcus aureus*:** cloxacillin

Pseudomonas aeruginosa: cold compresses, analgesics, elevation of feet

ERYTHEMA NODOSUM occurs in brucellosis, coccidioidomycosis, leptospirosis, toxoplasmosis, tuberculosis, 18% of cases of yersinosis, and in *Pasteurella, Streptococcus* and *Mycoplasma pneumoniae* infections; may also be due to contraceptive pills, malignant disease, sarcoidosis, sulphonamides, ulcerative colitis

ERYTHEMA CHRONICUM MIGRANS

Agent: *Borrelia burgdorferi*

Diagnosis: pruritic, erythematous papule or ring at location of tick bite, giving large, erythematous, macular, non-scaling, centrifugally spreading ring with trailing cast to 35 cm diameter, fading; biopsy

Treatment: tetracycline

ERYTHEMA INFECTIOSUM (FIFTH DISEASE)

Agent: *human parvovirus B19*

Diagnosis: clinical ('slapped cheek' appearance; maculopapular, vesicular or petechial rash may be present; joint symptoms, numbness and tingling in fingers; incubation period 4-14 d; children and adults; summer, early autumn; duration 2-5 d); dot hybridisation and capture ELISA of serum; PCR

Treatment: none

ERYTHEMA MARGINATUM: occurs in 10% of cases of acute rheumatic fever

Agent: immunomediated reaction to preceding infection with *Streptococcus pyogenes*

Diagnosis: roughly circular lesions spreading centrifugally at the same time as they clear centrally and producing a serpiginous outline; anti-streptolysin O, anti-DNAse B, anti-hyaluronidase, streptozyme

Prophylaxis: benzathine penicillin 1.2 MU (< 6 y: 600,000 U) i.m. at 4 weekly intervals, phenoxymethylpenicillin 250 mg (child: 125 mg) orally 12 hourly, sulphadiazine (< 27 kg: 500 mg orally once daily; ≥ 27 kg: 1 g orally daily), erythromycin 250 mg orally 12 hourly; continue until patient in early twenties and until 5 y have elapsed since last attack of rheumatic fever

ERYTHEMA MUTLIFORME/STEVENS-JOHNSON SYNDROME

Agents: coxsackievirus A9, 10, 16, B4, 5, echovirus 6, 11, *Mycoplasma pneumoniae;* numerous antibiotics

Diagnosis: clinical

Treatment: careful fluid management and wound care

Hemorrhagic Rash

Agents: several arboviruses, rickettsioses (typhus), spotted fevers (in 49% of cases (13% in first 3 d) of Rocky Mountain spotted fever), atypical measles (petechial over face, blanching)

Diagnosis: clinical; serology

Treatment:

Viruses: non-specific

***Rickettsia*:** tetracycline, doxycycline, chloramphenicol, cotrimoxazole

Macular Rash

Agents: *Ross River virus* (arms, palms, feet), St Louis encephalitis (transient, extremities), *human coxsackievirus B1, 2, 5*, *human echovirus 2, 4, 5, 13, 14, 17-19, 30*, *human enterovirus 71*, *Reoseolovirus*, *Rickettsia* (typhus), spotted fevers, *Mycoplasma pneumoniae* (mainly on arms, legs, trunk and face), pityriasis (desquamating); also niacin-associated illness (on face or upper arms)

Diagnosis: culture of serum; serology

Treatment:

Viruses: non-specific

***Rickettsia*:** tetracycline, doxycycline, chloramphenicol, cotrimoxazole

Pityriasis: selenium sulphide, sodium thiosulphate, ketoconazole

Maculopapular Rash

Agents: measles, atypical measles, rubella, *human echovirus 1-7, 11, 13, 14, 16-19, 25, 27, 30, 33, echo 9 virus, human parechovirus 1*, *human coxsackievirus A2, A4-A7, A9, A10, A16, B1-B5, enterovirus 71*, several arboviruses (including 31% of cases of dengue), infectious mononucleosis, *Reovirus*, adenovirus, roseola, erythema infectiosum, *Rotavirus*, *Chromobacterium violaceum*, *Pseudomonas aeruginosa* whirlpool-associated dermatitis, rickettsioses (including Mediterranean spotted fever and 82% of cases (46% in first 3 d) of Rocky Mountain spotted fever), *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Treponema pallidum subsp pallidum*, *Yersinia enterocolitica*, *Yersinia pseudotuberculosis, Mycoplasma pneumoniae, Trichinella spiralis* (in 70% of cases)

Diagnosis: viral culture of throat washings, throat swab, nasal swab; cytology of Koplik spots; serology; histology and immunofluorescence of skin biopsy; bacterial culture of skin lesions, blood; muscle biopsy

Measles: confluent, on face, spreading to extremities; very characteristic; conjunctivitis ++, rhinitis +, enanthem +, pharyngitis absent; incubation period 10-14 d; children, occasionally adults; winter, spring; duration 7-10 d; IgM antibody

Atypical Measles: over entire body

Rubella: faint, even non-existent; incubation period 12-23 d; children, occasionally adults; spring; duration 3-5 d; conjunctivitis ±, pharyngitis ±, rhinitis ±, enanthem ±; IgM antibody

Enteroviruses: pharyngitis ±, rhinitis ±, conjunctivitis and enanthem absent; virus isolation

Arboviruses: diffuse; extremities, torso, face

Infectious Mononucleosis: pharyngitis +, conjunctivitis, rhinitis and enanthem absent

***Chromobacterium violaceum*:** all skin surfaces except face, hands, feet

***Pseudomonas aeruginosa*:** becoming vesiculopustular

Mediterranean Spotted Fever: on trunk and extremities in 99% of cases, on palms and soles in 89%

***Neisseria*:** nonsymmetrical, scattered

***Mycoplasma pneumoniae*:** measles-like confluent or rubella-like discrete

Treatment:

Viruses: non-specific

***Chromobacterium violaceum*:** chloramphenicol

***Rickettsia*:** tetracycline, doxycycline, chloramphenicol, cotrimoxazole

***Neisseria*:** penicillin

***Pseudomonas aeruginosa*:** usually none required; silver nitrate or silver sulphadiazine if required

Yersinia: gentamicin, cefotaxime, doxycycline or ciprofloxacin if invasive disease

***Mycoplasma pneumoniae*:** doxycycline, tetracycline, erythromycin

***Trichinella spiralis*:** mebendazole

Roseola (Exanthema Rubitum)

Agents: *human herpesvirus 6*, *human coxsackievirus A6, A9, B1, B2, B4, B5*, *human echovirus 11, 16, 25, 27, 30*, *echo 9 virus*, adenovirus, parainfluenza, measles vaccine virus

Diagnosis: maculopapular rash appears as fever falls; conjunctivitis ±, rhinitis ±, pharyngitis and enanthem absent; incubation period 10-15 d; infants; spring, autumn; duration 5-7 d; serology

Treatment: non-specific

Fine Rash

Agents: atypical measles (on arms, spreading to trunk and face), chromobacteriosis (generalised)
Diagnosis: clinical; epidemiological; viral culture of throat swab or washings; blood cultures; serology
Treatment:

Atypical Measles: supportive
Chromobacteriosis: chloramphenicol

Polymorphous Rash

Agents: atypical measles (petechial, maculopapular, pustular component), erythema infectiosum (maculopapular, vesicular, petechial or absent), *Neisseria gonorrhoeae* (maculopapular, vesicular), *Neisseria meningitidis* (maculopapular, vesicular), *Salmonella*, Kawasaki syndrome (in 90% of cases; nonvesicular or crusting), *Pseudomonas aeruginosa* (nonpruritic to intensely pruritic, maculcopapular, vesiculopapular, vesicular, pustular)
Diagnosis: clinical; immunofluorescent antibody testing on serum and CSF; bacterial culture of skin lesions; blood cultures
Treatment:

Atypical Measles: supportive
***Neisseria*:** penicillin
***Salmonella*:** chloramphenicol
***Pseudomonas aeruginosa*:** usually none required; topical 0.1% polymyxin B or washing with antibacterial soap followed by topical alcohol-based drying lotion if required

Pruritic Rash

Agents: caterpillar contact (on arms in 75% of cases, on neck in 23%, on legs in 21%), cercarial dermatitis (bather's itch, clam-digger's itch, hunter's itch, lakeside disease, rice-paddy itch, sawah itch (Bahasa, Malaysia), schistosome dermatitis, sea bather's itch, swimmer's itch; *Austrobilharzia* spp, *Gigantobilharzia* spp, *Heterobilharzia americana, Orientobilharzia* spp, *Schistosoma bovis, Schistosoma mattheei, Schistosoma spindale, Schistosomatium douthitti, Trichobilharzia* spp), grain itch (*Pyemotes*); similar reactions may occur to fleas (*Ctenocephalides canis* from dogs, *Ctenocephalides felis* from cats, *Pulex irritans* from man), bedbugs, *'Ornithonyssus bursa'* (bird mite, paper mite), *Ornithonyssus sylvarum* (Northern fowl mite), *'Ornithonyssus bacoti'* (tropical rat mite), *Dermanyssus gallinae* (chicken mite), *Dermanyssus hirudinis* (from cage birds, swallows), *Tyrophagus* (bulb mites; from foods), *Glycyphagus domesticus* (house itch mite), *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (house-dust mites), *'Trombicula autumnalis'* (from vegetation), *Haloclava producta* (ghost anemone dermatitis)
Diagnosis: patient history

Cercarial Dermatitis: produced in sensitised persons as a result of penetration of skin by cercariae, which subsequently die but cause irritation, pruritus, macules and papules at site of penetration; demonstration of *Schistosoma*-infected snails at site of exposure

Grain Itch: thin-walled central vesicles and erythematous areolae on torso and extremities, spreading to face and resolving to hypopigmented macules; demonstration of *Pyemotes* on patient or in environment (vegetation, grain, wood)
Treatment: antihistamines, antipruritics

Caterpillar Contact: remove affected clothing; remove hairs by applying adhesive tape and immediately pulling off

Grain Itch and Other Infestations: lindane to skin; pyrethrin-based fogging

Pustular Rash

Agent: *Pseudomonas aeruginosa* whirlpool-associated dermatitis
Diagnosis: culture of skin lesions
Treatment: usually none required; topical 0.1% polymyxin B or washing with antibacterial soap followed by topical alcohol-based drying lotion if required

Splotchy Rash

Agent: *Chlamydia psittaci* (face and neck)
Diagnosis: clinical; serology
Treatment: erythromycin, tetracycline

Generalised Urticarial Rash

Agents: *human coxsackievirus A9, A16, B4, B5, echovirus 11*, *Mycoplasma pneumoniae*; hypersensitivity reaction to foods or drugs or local irritants
Diagnosis: appearance (*Mycoplasma pneumoniae* papular or giant), history; serology
Treatment:

Viruses: non-specific
***Mycoplasma pneumoniae*:** doxycycline, erythromycin
Hypersensitivity: withdrawal of reactant, antihistamines

VESICULAR RASH

Agents: simplexvirus 3 (shingles, chickenpox; worldwide; usually a mild disease, but serious disease in population with no previous exposure and in immunocompromised; in 25% of patients with Hodgkin's disease and 3% of patients with solid tumours; trunk, extremities, palms, fingers), *human coxsackievirus A4, A5, A7-A10, A16, B1, B3, B5* and *human enterovirus 71* (hand, foot and mouth syndrome), *human echovirus 5, 6* (zoster-like rash), *9, 11, 17*, erythema infectiosum, neonatal *simplexvirus* 1 and 2 infection (papulovesicular), smallpox, monkeypox, *Pseudomonas aeruginosa* whirlpool-associated dermatitis, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Mycoplasma pneumoniae* (varicella-like; legs, trunk, face)

Diagnosis: bacterial and viral culture of vesicle fluid and scrapings; viral culture of feces, throat swab; cytology (Tzanck smear stained with Paragon Multiple stain simple, inexpensive and easy to interpret) of scraping from base of vesicle; immunofluorescence; complement fixation test, hemagglutination inhibition, neutralisation; histology of biopsy; electron microscopy of skin lesions, vesicle fluid or pus; gel diffusion of vesicle fluid or pus

Simplexvirus 3: direct fluorescent antibody staining of cells scraped from ulcerative lesions; characteristic multinucleate giant cells in vesicles seen histologically; visualisation of virus in vesicles by electron microscopy; virus isolation

Poxviruses: antigen detection

Treatment:

Simplexvirus 1* and *2: aciclovir, penciclovir

Simplexvirus 3: saline packs 12 hourly for 10 min, calamine lotion 12 hourly, povidone iodine 6 hourly topically; oral antibiotics according to bacteriology of superinfection

Varicella in Normal Patient With Pneumonitis or Encephalitis or in Immuncompromised: aciclovir 10 mg/kg i.v. 8 hourly, each infusion administered over a period of 1 h, for 7-10 d (adjust dose for renal function)

Herpes Zoster in Immunocompromised and in Any Patient Seen Within 72 h of Onset of Vesicles: famciclovir 250 mg orally 8 hourly for 7 d, valaciclovir 1 g orally 8 hourly for 7 d, aciclovir 20 mg/kg to 800 mg orally 5 times daily for 7 d; prednisolone 40 mg orally daily for 10 d, tapering off over 2 w, may be useful in averting or reducing post-herpetic neuralgia; herpes zoster neuralgia may be treated with nortriptyline, gabapentin, sustained release oxycodone or topical lidocaine patches

Other Viruses: non-specific; discontinue steroids

Neisseria: penicillin

Pseudomonas aeruginosa: usually none required; topical 0.1% polymyxin B or washing with antibacterial soap followed by topical alcohol-based drying lotion if required

ROSE SPOTS

Agent: *Salmonella* (enteric fever, 15% of cases of *Salmonella* brain abscess)

Diagnosis: clinical; culture of feces, blood, bone marrow; computerised axial tomography, radionuclide scan, culture and histology of brain biopsy where indicated

Treatment: chloramphenicol

PETECHIAL OR PURPURIC RASH

Agents: *human coxsackievirus A4, A9* (anaphylactoid), *B2, 5, human echovirus 3, 4, 7* (anaphylactoid), *18* (anaphylactoid), *Mycoplasma pneumoniae* (rare)

Diagnosis: clinical; serology

Treatment: supportive

Mycoplasma pneumoniae: doxycycline, erythromycin

PAPULAR-PURPURIC GLOVES AND SOCKS SYNDROME

Agent: *human parvovirus B19*

Diagnosis: pruritic erythema with edema, papular-purpuric lesions of hands and feet with sharp demarcation at wrists and ankles, lymphadenopathy, mucosal lesions, asthenia, anorexia, fever, arthralgias, mild anemia, leucocytosis or leucopoenia, transient neutropenia; IgM, IgG seroconversion, serum PCR

Treatment: supportive

NON-SPECIFIC RASH is also seen in 40% of cases of Q fever endocarditis, 15% of acute viral hepatitis cases, 11% of enterovirus infections (conjunctivitis and enanthem absent, pharyngitis ±, rhinitis ±), in 6% of infectious mononucleosis cases due to *Epstein-Barr virus* (rarely in *human cytomegalovirus* cases, occasionally in *Toxoplasma gondii* syndromes), in 2% of cases of influenza A, in *human adenovirus B serotype 16* (but not *human adenovirus E serotype 4*) infections, in aseptic meningitis, in infections with *human coxsackievirus A2, A4, A9, A16* and *B4*, in *Staphylococcus aureus* endocarditis and toxic erythema, and in infections with dermatophytes; also in dermatomyositis (over extensor surfaces of finger joints and over large joints, heliotrope rash of eyelids), and in reactive states to local application of chemicals or to ingestion of drugs (conjunctivitis, pharyngitis, rhinitis and enanthem absent), other chemicals or foods

(An exanthem and pulmonary involvement may be seen in infections with *human adenovirus B serotype 7*, *human adenovirus 7a*, *simplexvirus 1*, *simplexvirus 3*, *Epstein-Barr virus*, *human coxsackievirus A9*, *human echovirus 11*, *mammalian orthoeovirus type 3*, *measles virus*, *Chlamydia psittaci, Mycoplasma pneumoniae, Neisseria meningitidis, Mycobacterium tuberculosis, Histoplasma capsulatum, Cryptococcus neoformans, Coccidioides immitis*)

PARONYCHIA

Agents: *Candida albicans*, *Pseudomonas aeruginosa* (may lead to 'green nail syndrome'), *Staphylococcus aureus*, *Streptococcus*, anaerobes, *Haemophilus paraprophilus*, *Eikenella corrodens*, *Fusarium* (neutrophilia)

Diagnosis: culture of pus swab

Treatment: avoidance of precipitating factors (beer, milk, perspiration, water immersion, etc); topical povidone iodine paint, magenta paint, clioquinol cream; antibiotics as for **CELLULITIS** if present

Candida: miconazole 2% tincture twice daily for 5-7 d

Chronic or Unresponsive: fluconazole 50 mg orally daily for at least 2 w, itraconazole 100 mg orally daily for at least 2 w, ketoconazole 200 mg orally once daily for at least 2 w

Fusarium: nail removal, amphotericin B 1.25 mg/kg daily + 5-flucytosine

Pseudomonas aeruginosa: 0.25-1% acetic acid, 0.1% polymyxin B

Staphylococcus aureus: di/flucloxacillin 25 mg/kg to 500 mg orally 6 hourly, cephalexin 12.5 mg/kg to 500 mg orally 6 hourly

HERPETIC WHITLOW

Agent: *simplexvirus 1*

Diagnosis: may masquerade as acute pyogenic infection; swab culture

Treatment: valaciclovir 500 mg orally 12 hourly for 7-10 d, famciclovir 250 mg orally 12 hourly for 7-10 d, aciclovir 5 mg/kg to 200 mg orally 5 times daily for 7-10 d

DANDRUFF

AGENT: ? *Malassezia* spp

Diagnosis: clinical

Treatment: selenium sulphide shampoo

OTITIS EXTERNA: 0.6% of new episodes of illness in UK; 0.4% of ambulatory care visits in USA; most common cause of localised area pain

Agents: includes 'swimmer's ear' (acute diffuse otitis externa) due to infections with *Pseudomonas aeruginosa* (35-70% of all cases of otitis externa), *Proteus* (2% of all cases), *Escherichia coli* (2% of all cases), *Klebsiella pneumoniae* (2% of all cases), other coliforms, *Alcaligenes, Vibrio alginolyticus, Vibrio mimicus* (after exposure to sea water), *Aeromonas*; acute localised otitis externa due to *Staphylococcus aureus* (16% of all cases), coagulase negative *Staphylococcus* (7% of all cases), group C *Streptococcus* (0.8% of all cases), *Streptococcus pyogenes*; otomycosis due to *Candida albicans* (7% of all cases), *Aspergillus fumigatus, Aspergillus flavus* and *Aspergillus niger* (primary or secondary to eczemoid reactions), *Scedosporium*; very rare specific infections with *Mycobacterium* species (including *Mycobacterium tuberculosis*), *Corynebacterium diphtheriae* and *Actinomyces israelii*; mixed infections due to obligate anaerobes (*Peptostreptococcus, Propionibacterium acnes, Fusobacterium necrophorum, Bacteroides, Porphyromonas asaccharolytica, Prevotella intermedia)* and Gram negatives in chronic conditions (29% of total cases); and malignant (necrotising) otitis externa (infection spreads to temporal bone, zygomatic bone and bones at base of skull, causing cranial neuropathies and significant mortality) due to *Pseudomonas aeruginosa* (rarely, *Aspergillus fumigatus, Klebsiella oxytoca, Proteus mirabilis, Staphylococcus aureus,* coagulase negative *Staphylococcus*) in elderly and diabetics; allergy and sensitivity reactions (eczema, psoriasis, seborrheic dermatitis, lupus erythematous) may simulate infection

Diagnosis: itch, otorrhoea, pain varying from moderate to severe; hearing loss may occur if auditory canal occluded by lesion; culture of ear swab

Malignant Otitis Externa: > 60 y, diabetes mellitus; otalgia in 75-100%, headache (usually temporal or occipital and often excruciating), periauricular tenderness and swelling, profuse purulent otorrhoea, edema and erythema of ear canal, granulation tissue in external auditory canal; facial nerve palsy late complication; raised ESR (often > 100 mm/h); computerised axial tomography or magnetic resonance imaging; isolation of organism from external auditory canal or mastoid

Treatment: relieve pain with codeine or, if severe, pethidine or morphine; clean auditory canal by suction (do not syringe) or dry mopping with cotton wool on a thin carrier (not cotton bud); at least daily toilet with acetic acid 0.25% or povidone iodine 0.5% solution

Swimmer's Ear (Acute Diffuse Otitis Externa): dexamethasone 0.05% + framycetin sulphate 0.5% + gramicidin 0.005% ear drops 3 drops 3 times daily or as wick soaked in combination for 3-7 d; flumethasone 0.02% + clioquinol 1% ear drops 3 drops instilled into ear after cleaning twice daily or as wick soaked in combination for 3-7 d; triamcinolone/neomycin/gramicidin/nystatin combination 2-3 drops twice daily or inserted as saturated gauze wick; avoidance of swimming during attack; use of acetic acid + isopropyl alcohol or acetic acid + benzedthonium chloride 4-6

drops instilled into each ear after shaking water out following water immersion, or insertion of plugs of nonabsorptive material (eg., paraffin-impregnated cotton wool) may help prevent recurrence

Acute Localised Otitis Externa: di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly for 5 d

Aspergillus: if eardrum intact, clean with alcohol, then instil 2 drops 4% boric acid in 5% alcohol 6 hourly for up to 3 w

Malignant Otitis Externa:

Pseudomonas aeruginosa: gentamicin 5-7 mg/kg i.v. daily (child: 7.5 mg/kg i.v. in 1-3 divided doses) + ticarcillin-clavulanate 50 mg/kg to 3 g i.v. 4-6 hourly or ceftazidime 25 mg/kg to 1 g i.v. 8 hourly; ciprofloxacin 1.5-2.5 g/d orally for 6-10 w; piperacillin 3-4 g i.v. 4-6 hourly + tobramycin 1.3 mg/kg i.v. 8 hourly for 4-8 w

Aspergillus: incision and drainage of pinna; itraconazole 200 mg/d for 3 mo, amphotericin B ± flucytosine

Staphylococcus aureus: as for **Swimmer's Ear**; if severe, flucloxacillin 500 mg orally 6 hourly (< 2 y: ¼ dose; 2-10 y: ½ dose), erythromycin 500 mg orally 6 hourly (child: 30-50 mg/kg daily in divided doses)

Candida albicans: cleansing; clotrimazole lotion 3 drops 8 hourly for 7 d, econazole 1% solution 2 drops 12 hourly

Mycobacterium: streptomycin, paraminosalicylic acid or other anti-tuberculous drugs depending on susceptibility of isolates

Corynebacterium diphtheriae: antitoxin + penicillin, cephalosporin, erythromycin

Actinomyces israelii: penicillin ± streptomycin; tetracycline, erythromycin, cephalosporin

Others: penicillin, chloramphenicol, ticarcillin, metronidazole

Wound and Soft Tissue Infections, Local and Generalised Sepsis

HUMAN BITE AND CLENCHED FIST INFECTIONS: human bites 2-23% of all bite wounds; 15-20% on head and neck

Agents: *Fusobacterium*, β-lactamase-producing anaerobes, *Eikenella corrodens, Enterobacter, Klebsiella, Streptococcus,* diphtheroids, *Neisseria*, coagulase negative *Staphylococcus*, *Pseudomonas, Proteus, Escherichia coli, Staphylococcus aureus, Haemophilus influenzae*

Diagnosis: culture of wound swab

Treatment: forced pulsatile irrigation of wound, debridement, scrubbing with 1% povidone iodine; elevation; immobilisation; do not suture or surgically close wound before 24 h post injury; procaine penicillin 50 mg/kg to 1.5 g i.m. as single dose, then amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for 5 d; assess tetanus immune status and administer tetanus toxoid if no history of 3 or more doses of toxoid in previous 5 y, and tetanus immunoglobulin if uncertain vaccination history or < 3 doses of toxoid

Established Infection: metronidazole 10 mg/kg to 400 mg orally 12 hourly for 5-10 d + ceftriaxone 25 mg/kg to 1 g i.v. daily for 5-10 d or cefotaxime 25 mg/kg to 1 g i.v. 8 hourly for 5-10 d; piperacillin-tazobactam 100/12.5 mg to 4/0.5 g i.v. 8 hourly for 5-10 d; ticarcillin-clavulanate 50/1.7 mg/kg to 3/0.1 g i.v. 6 hourly for 5-10 d

Penicillin Hypersensitive: metronidazole 10 mg/kg to 400 mg orally 12 hourly for 5-10 d + doxycycline 5 mg/kg to 200 mg first dose then 2.5 mg/kg to 100 mg orally daily for 5-10 days (not < 8 y, pregnant or breastfeeding) or cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly for 5-10 d or ciprofloxacin 10 mg/kg to 500 mg orally 12 hourly for 5-10 d

CAT AND DOG BITE INFECTIONS

Agents: *Pasteurella multocida* (> 50% of cat bites, 15-30% of dog bites), *Staphylococcus aureus* (20-30% of dog bites), other *Pasteurella* species, *Capnocytophaga canimorsus, Capnocytophaga cynodegmi, Streptomyces sp EF-4*, *Streptomyces coelicolor*, *Actinobacillus actinomycetemcomitans*, *Haemophilus aprophilus*, *Staphylococcus intermedius* and other coagulase negative *Staphylococcus*, *Streptococcus* (α, β and γ), *Micrococcus, Actinomyces, Fusobacterium, Peptostreptococcus, Eubacterium, Veillonella parvula, Leptotrichia buccalis,* rarely Gram negative enteric bacilli, *Pseudomonas fluorescens, Francisella tularensis,*CDC Group NO-1

Diagnosis: culture of wound swab

Treatment: as for **HUMAN BITE AND CLENCHED FIST INFECTIONS**, but suture or delayed primary closure may be performed

FISH SPINE INJURY AND OTHER WATER-RELATED INFECTIONS

Agents: *Vibrio* species (especially *Vibrio vulnificus*, *Vibrio alginolyticus*; rapidly developing life-threatening infection may occur in cirrhosis or iron overload), *Shewanella putrefaciens* (salt or brackish water), *Aeromonas hydrophila* (fresh or brackish water; high risk of fulminant infection in hepatic disease, chronic illness, immunocompromised), *Edwardsiella tarda* (similar to *Aeromonas*), *Pseudomonas* species, *Klebsiella, Escherichia, Staphylococcus* species, *Streptococcus pyogenes* (often associated with coral cuts), *Mycobacterium marinum* (fish tanks)

Diagnosis: swab culture

Treatment: irrigation, exploration; tetracycline + broad spectrum β-lactamase-stable β-lactam or narrow spectrum β-lactamase-stable penicillin + gentamicin

***Vibrio*:** incision, drainage, debridement; doxycycline 5 mg/kg to 200 mg orally or i.v. twice daily then 2.5 mg/kg to 100 mg orally or i.v. 12 hourly (not < 8 y); ceftazidime 2 g i.v. 3 times a day; cefotaxime; ceftriaxone; ciprofloxacin 400 mg twice a day for 3 d, minocycline

***Aeromonas hydrophila, Edwardsiella tarda*:** ciprofloxacin 10 mg/kg to 400 mg i.v. or 10 mg/kg to 500 mg orally 12 hourly

***Streptococcus pyogenes*:** phenoxymethylpenicillin 500 mg orally 6 hourly

BURN INFECTIONS

Agents: *Pseudomonas aeruginosa* (only in burns affecting ≥ 50% of total body surface and involving destruction of cutaneous structures), *Staphylococcus aureus*, *Acinetobacter*, *Flavobacterium meningosepticum*, other bacteria, *Aspergillus*; all isolates should be considered of possible significance

Diagnosis: Gram stain, quantitative culture (> 10^5/g = sepsis) and histology of biopsy

Treatment: early and frequent debridement of necrotic tissue

***Flavobacterium meningosepticum*:** ciprofloxacin, clindamycin

Pseudomonas aeruginosa: mafenide; parenteral aminoglycoside + β-lactam if frank infection

Other Bacteria: gentamicin; topical povidone iodine; nonsteroidal antiinflammatory drugs

Aspergillus: i.v. amphotericin B; radical debridement/amputation essential for management

SURGICAL PROPHYLAXIS: The most important single factor in preventing infection is the surgeon's technique. Others are short preoperative hospital stay; preoperative bathing and showering with antibacterial soap; no shaving or shaving to take place immediately before operation; reduction of risk factors such as obesity, diabetes, malnutrition; spraying of wounds with povidone iodine; postoperative vitamin C. Nasal application of mupirocin in *Staphylococcus aureus* carriers may reduce risk of nosocomial infection. Risk factors for surgical wound infection include prolonged preoperative stay, old age, morbid obesity, infection at other sites, ASA class, disease severity index, immunosuppression, razor shave, low abdominal incision, no prophylactic antibiotics, specific procedure, intraoperative contamination, prolonged duration of surgery, surgical wound class; probably malnutrition, low albumin, prolonged admission, tissue trauma, multiple procedures; possibly cancer, diabetes mellitus, inexperienced surgeon, low procedure volume, number of people in operating room, emergency surgery, no preoperative scrub, failure to obliterate dead space, poor hemostasis, foreign material, glove puncture, drains. Antibiotics should be administered systemically at start of anesthesia and, except where indicated, when skin sutures are being inserted.

Insertion of Synthetic Biomaterial Device or Prosthesis, Clean Operations in Patients with Impaired Host Defences (Likely Pathogens *Staphylococcus aureus*, Coagulase Negative *Staphylococcus, Escherichia coli*): cefazolin 1 g i.v. or cefuroxime 750 mg i.v. 30 mins before skin incision, second dose if procedure > 3 h

Clean Wounds (Elective, Primarily Closed, No Acute Inflammation or Transection of Genitourinary, Oropharyngeal, Gastrointestinal, Biliary or Tracheobronchial Tracts; No Technique Breaks): exogenous infection, especially *Staphylococcus*; infection rate < 2%

Cardiac Surgery (Valve Replacement, Coronary Artery Bypass Surgery, Cardiac Transplant, Insertion of Permanent Pacemaker), Peripheral Vascular Procedures, Arterial Reconstructive Surgery of Abdominal Aorta or Lower Limb (Likely Pathogens *Staphylococcus aureus*, Coagulase Negative *Staphylococcus*, Diphtheroids, Aerobic Gram Negative Bacilli), Breast (Likely Pathogen *Staphylococcus aureus*), Dialysis Access (Likely Pathogens Coagulase Negative *Staphylococcus*, *Staphylococcus aureus*): cephalothin 50 mg/kg to 2 g i.v. at time of induction (continue 6 hourly for 48 for arterial reconstructive surgery involving abdominal aorta or lower limb); cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) i.v. at time of induction (continue 8 hourly for 48 h for arterial reconstructive surgery involving abdominal aorta or lower limb); gentamicin 2 mg/kg i.v. at time of induction (continue 6 hourly for 48 h for arterial reconstructive surgery involving abdominal aorta or lower limb) + di(flu)cloxacillin 50 mg/kg to 2 g i.v. at time of induction (continue 6 hourly for 48 h for arterial reconstructive surgery involving abdominal aorta or lower limb); vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1.5 g i.v. over at least 1 h, ending infusion just prior to induction + gentamicin 2 mg/kg i.v. at time of induction

Orthopedic (Prosthetic Large Joint Replacement, Insertion of Prosthetic or Transplant Material, Internal Fixation of Fractures of Large Bones): likely pathogens *Staphylococcus aureus*, coagulase negative *Staphylococcus,* diphtheroids, aerobic and anaerobic Gram negative bacilli; cephalothin 50 mg/kg to 2 g i.v. at time of induction, or cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) i.v. at time of induction

Craniotomy (Prolonged Procedures, Reexplorations, Microsurgery, Insertion of Prosthetic Material), Clean Head and Neck Surgery (Skin Excision, Neck Dissections): likely pathogens coagulase negative *Staphylococcus*, *Staphylococcus aureus*, diphtheroids, less commonly aerobic Gram negative bacilli and anaerobes; di(flu)cloxacillin 50 mg/kg to 2 g i.v. at time of induction, cephalothin 50 mg/kg to 2 g i.v. at time of induction, cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) i.v. at time of induction; vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1.5 g i.v. by slow infusion ending just before procedure if MRSA known or suspected or penicillin hyersensitive

Clean-contaminated Wounds (Urgent or Emergency Case That is Otherwise 'Clean'; Elective, Controlled Opening of Gastrointestinal, Oropharyngeal, Biliary or Tracheobronchial Tract; Minimal Spillage and/or Minor Technique Break; Reoperation Through 'Clean' Incision Within 7 d; Blunt Trauma, Intact Skin; Negative Exploration): endogenous bacteria > 10^6/g of tissue; infection rate 5-10%

Head, Neck (Including Ear, Nose, Throat and Dental Procedures, Laryngectomy and Other Head and Neck Cancer Operations) and Thoracic Surgery: likely pathogens mixed aerobic and anaerobic upper respiratory flora, *Staphylococcus aureus*; cephalothin 50 mg/kg to 2 g or cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) at time of induction

Mandibular Fractures (Likely Pathogens Oral Flora): penicillin 2 MU (4 MU if > 60 kg) i.v. 30 mins before skin incision

Colorectal, Appendicectomy, Upper Gastrointestinal Tract, Biliary Surgery, Laparoscopic Surgery (All Persons): likely pathogens anaerobic streptococci, *Enterococcus faecalis*, enteric aerobic and anaerobic Gram negative bacilli, clostridia; 10% mannitol clearance; metronidazole 1 g rectally 2-4 h before surgery or 12.5 mg/kg to 500 mg i.v. ending infusion at time of induction (omit for patients with normal gastric acid and motility, no obstruction, no bleeding and no malignancy or previous gastric surgery undergoing upper gastrointestinal surgery and for

patients < 60 y and non-diabetic undergoing biliary tract surgery and for elective cholecystectomy with low risk of exploration of common bile duct) + cephalothin 50 mg/kg to 2 g or cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) i.v. or gentamicin 2 mg/kg i.v. at time of induction; cefoxitin 40 mg/kg to 2 g i.v. at time of induction as single drug

Endoscopic Procedures Involving Biliary Tract, Sclerotherapy, Esophageal Dilation, Endoscopic Retrograde Cholangiopancreatography, Percutaneous Endoscopic Gastrostomy, Jejunostomy Tube Insertion: cephalothin 50 mg/kg to 2 g i.v. at time of induction or cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) i.v. or gentamicin 2 mg/kg i.v. at time of induction; if endoscopic retrograde cholangiopancreatography and biliary stasis, + amoxycillin + clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 12 hourly for 3 d

Beta-lactam Allergy or MRSA Colonisation: vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1.5 g i.v. by slow infusion ending just before the procedure

Hernia Repair with Prosthetic Maaterial: cephalothin 50 mg/kg to 2 g i.v. at time of induction, cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) i.v. at time of induction

Hysterectomy, Termination of Pregnancy (All Women): screen for vaginosis and *Chlamydia trachomatis* and treat before operation; otherwise, likely pathogens anaerobic bacteria, enteric Gram negative bacilli, *Streptococcus, Enterococcus*; tinidazole 2 g orally 6-12 h prior to surgery or metronidazole 500 mg i.v. ending infusion at time of induction + cephalothin 2 g i.v. at time of induction or cephazolin 1 g i.v. at time of induction (doxycycline 100 mg i.v. if β-lactam allergy) or cefoxitin 40 mg/kg to 2 g i.v. at time of induction

Caesarean Section: likely pathogens anaerobic bacteria, *Enterococcus faecalis*, aerobic Gram negative bacilli, streptococci; cephalothin 2 g i.v. or cephazolin 1 g (≥ 80 kg: 2 g) i.v. immediately after clamping cord; β-lactam allergy: clindamycin 900 mg i.v. + gentamicin 1.5 mg/kg i.v. at time of cord clamping

Urinary Tract Surgery: likely pathogens *Enterococcus faecalis*, enteric Gram negative bacilli; not needed for patients with sterile urine; patients with urinary tract infection should be treated preoperatively on basis of culture and susceptibility results; if this is not possible, gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. single dose (adjust dose for renal function)

Renal Transplantation: likely pathogens *Staphylococcus*, *Streptococcus*, enteric Gram negative bacilli; cephalothin 2 g or cephazolin 1 g i.v. or cefuroxime 750 mg i.v. at time of induction

Liver Transplantation: likely pathogens *Staphylococcus, Streptococcus,* enteric Gram negative bacilli, *Enterococcus*; cephalothin 2 g or cephazolin 1 g i.v. at time of induction + metronidazole 500 mg i.v. at time of induction; cefotetan 2g or cefoxitin 2 g i.v. at time of induction; ampicillin-sulbactam 3 g i.v. 30 mins before skin incision (second dose if procedure > 3 h)

Pancreas or Pancreas/Kidney Transplantation: likely pathogens coagulase negative staphylococci, *Enterococcus,* yeasts; ampicillin-sulbactam 3 g i.v. + fluconazole 400 mg i.v. 30 mins before skin incision

Lower Limb Amputation Surgery: likely pathogen *Clostridium perfringens;* benzylpenicillin 30 mg/kg to 1.2 g i.v. at time of induction then 6 hourly for 24 h, metronidazole 1 g rectally commencing 2-4 h before surgery or 12.5 mg/kg to 500 mg i.v. ending at time of induction then 12 hourly for 24 h; iodine skin antisepsis

Prostatectomy: likely pathogens coliforms, staphylococci, *Pseudomonas;* gentamicin 2 mg/kg i.v. as a single dose at time of induction

Transrectal Prostatic Biopsy: trimethoprim 300 mg orally as single dose 1 h before procedure

Arterial Reconstructive Surgery Involving Abdominal Aorta and/or Lower Limb, Especially if Groin Incision Or Implantation of Foreign Material: cephalothin 50 mg/kg to 2 g i.v. at time of induction and then 6 hourly for 48 h, cephazolin 25 mg/kg to 1 g (≥ 80 kg: 2 g) i.v. at time of induction and then 6 hourly for 48 h, di/flucloxacillin 50 mg/kg to 2 g i.v. at time of induction and then 6 hourly for 48 h + gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) i.v. at time of induction and 24 h later (adjust dose for renal function)

Known or Suspected MRSA or Penicillin Hypersensitive: vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1.5 g i.v. by slow infusion ending just before procedure + gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) i.v. at time of induction and 24 h later (adjust dose for renal function)

Contaminated Wounds (Acute Non-purulent Inflammation; Major Technique Break or Major Spill from Hollow Organ; Penetrating Trauma < 4 h Old; Chronic Open Wounds to be Grafted or Covered): as for **Clean-contaminated Wounds**, but infection rate 12-20%

Dirty Wounds (Purulence or Abscess; Preoperative Perforation of Gastrointestinal, Oropharyngeal, Biliary or Tracheobronchial Tracts; Penetrating Trauma > 4 h Old): primary pathogen, endogenous organisms; surgical technique most important; delayed primary closure reduces infection rate from 50% to 0%

Ruptured, Perforated or Gangrenous Viscus: likely pathogens anaerobic bacteria, *Enterococcus faecalis*, aerobic Gram negative bacilli; tetracycline lavage; metronidazole 500 mg i.v. 8 hourly + amoxycillin 2 g 4 hourly + gentamicin 1.3 mg/kg 8 hourly

Fungal Prophylaxis in Critical Surgical Patients (≥ 3 d in Surgical ICU): fluconazole 400 mg/d

Burns (Extensive Skin Loss): likely pathogens *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, enteric Gram negative bacilli; silver sulphadiazine 1% with chlorhexidine gluconate 0.2% cream topically at each dressing change

Ophthalmic Surgery: likely pathogens *Staphylococcus aureus*, coagulase negative *Staphylococcus*, *Streptococcus viridans*; gentamicin or chloramphenicol eye drops or ointment for 1-2 d only

MUSCULAR, SKELETAL AND SOFT TISSUE TRAUMA, CRUSH INJURIES AND STAB WOUNDS

Agents: *Staphylococcus aureus*, *Streptococcus pyogenes*, *Clostridium perfringens,* aerobic Gram negative bacilli

Diagnosis: swab or tissue culture

Treatment: careful cleaning, debridement, immobilisation, elevation; tetanus toxoid if uncertain vaccination history, < 3 doses of tetanus toxoid, > 10 y since vaccination or 5-10 y and dirty or major wound; tetanus immunoglobulin if uncertain vaccination history or < 3 doses of tetanus toxoid and dirty or major wound

Hospitalisation Not Required: di(flu)cloxacillin 12.5-25 mg/kg to 500 mg orally 6 hourly for 5-7 d + metronidazole 10 mg/kg to 400 mg orally 12 hourly for 5-7 d

Hospitalisation Required: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin 5-7 mg/kg i.v. as single daily dose (child: 7.5 mg/kg/d i.v. in 1-3 divided doses)+ metronidazole 12.5 mg/g to 500 mg i.v. 12 hourly for at least 5 d; cephalothin 25 mg/kg to 2 g i.v. 6 hourly or cephazolin 15 mg/kg to 2 g i.v. 8 hourly + metronidazole as above; if possibility of gas gangrene, benzylpenicillin 60 mg/kg to 2.4 g i.v., repeating in 4 h if necessary

SUPPURATIVE WOUND INFECTIONS

Agents: organisms causing **LOCAL AND GENERALISED SEPSIS** in low numbers; low pathogenicity organisms such as coagulase negative *Staphylococcus*

Diagnosis: swab culture after microscopic screening; semiquantitative culture using plastic i.v. catheter on blood agar in surgical incisional wounds

Treatment: antibiotics usually not required; thorough cleansing; surgical drainage; irrigation with isotonic saline or isotonic stabilised 0.05% sodium hypochlorite 12 hourly; local antiseptics (10% mercurochrome or 1% chlorhexidine cream 12 hourly after bathing) or saline dressings

Postoperative:

Mild to Moderate with Surrounding Cellulitis: di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly for at least 5 d or cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for at least 5 d if penicillin hypersensitive; if Gram negative bacilli suspected or proven, amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for at least 5 d as single agent

Severe, Systemic Symptoms: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly or cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 50 mg/kg to 2 g i.v. 8 hourly if penicillin hypersensitive; if Gram negative bacilli suspected or proven, add gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. daily (adjust dose for renal function); if immediate penicillin hypersensitivyt or high incidence of MRSA, substitute vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly) for di/flucloxacillin, cephalothin or cephalzolin

Post-traumatic:

Clean Wounds Where Management Delayed or Debridement Difficult: di/flucloxacillin 12.5 mg/kg to 500 mg orally 6 hourly for 5 d + metronidazole 10 mg/kg to 400 mg orally 12 hourly for 5-7 d; amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for 5 d

Penicillin Hypersensitive (Not Immediate): substitute cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 5 d

Immediate Penicillin Hypersensitvity or Possible *Pseudomonas*: ciprofloxacin 10 mg/kg to 500 mg orally 12 hourly for 5 d + clindamycin 10 mg/kg to 450 mg orally 8 hourly for 5 d

Contaminated Wounds: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. daily (adjust dose for renal function) + metronidazole 12.5 mg/kg to 500 mg i.v. 12 hourly

Pencillin Hypersensitive (Not Immediate): metronidazole 12.5 mg/kg to 500 mg i.v. 12 hourly + cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 50 mg/kg to 2 g i.v. 8 hourly

Immediate Penicillin Hypersensitivity: gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function) + clindamycin 15 mg/kg to 600 mg i.v. or orally 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly

LOCAL AND GENERALISED SEPSIS: 750,000 cases/y in USA; sepsis = a systemic inflammatory response to infection; severe sepsis = sepsis with one or more dysfunctional organs or systems (death rate 30-35%); systemic inflammatory response syndrome = a syndrome in which inflammatory mediator release causes alterations in body temperature (> 38°C or < 36°C), heart rate > 90 beats/min, alterations in respiratory function (rate > 20 breaths/min or PO_2 < 32 mmHg, alterations in WBC count (> 12000/mm^3 or < 4000/mm^3 or > 10% immature forms); compensatory anti-inflammatory

response syndrome = syndrome in which anti-inflammatory mediator release overcompensates for the systemic inflammatory response; septic shock = severe sepsis with hypotension that is resistant to fluid resuscitation and requires pharmacological intervention (death rate ≈ 50%); multiple organ dysfunction syndrome = syndrome in which hypotension and hypoperfusion, secondary to pathophysiological alterations in severe sepsis, result in dysfunction in multiple organs

Agents: *Staphylococcus aureus* (always significant; 15% of hospital infections); *Streptococcus* (Groups A, C and G, others in hospital infections, *Streptococcus milleri* in abscesses; Group A 0.7% of hospital infections, Group B 2%, Group D 10%); coliforms (mainly in hospital-acquired infections, diabetics, immunosuppressed and severely debilitated patient; also in agricultural wounds; *Escherichia coli* 15% of hospital infections (83% of infections following major abdominal surgery), *Proteus* 7%, *Klebsiella* 5%, *Enterobacter* 4%); *Pseudomonas aeruginosa* (5% of hospital infections) and other *Pseudomonas* species; *Bacteroides fragilis* (3% of hospital infections, 73% of intraabdominal wounds); other anaerobes (other *Bacteroides*, *Clostridium*, *Peptococcus*; 7% of hospital infections, 85% of infections following major abdominal surgery); *Pasteurella; Vibrio vulnificus* (case-fatality rate 67% in primary sepsis, 22% in wound infections), *Vibrio cholerae*, *Vibrio mimicus, Vibrio parahaemolyticus, Vibrio alginolyticus, Vibrio damsela* and *Aeromonas* (trauma and exposure to water); *Yersinia pestis; Mycobacterium fortuitum*, *Mycobacterium chelonae* and *Mycobacterium smegmatis* (primary and post-surgical (especially cardiac) infections, catheter tunnel infections); *Mycobacterium haemophilum* (immunocompromised); *Chromobacterium violaceum*; *Campylobacter fetus* subsp *fetus* (abscesses); *Campylobacter concisus* (foot ulcer); *Clostridium botulinum; Achromobacter; Acinetobacter calcoaceticus; Eikenella corrodens* (55% of cases related to human bites or fist-fight injuries); *Corynebacterium jeikeium* (local infections at sites of biopsy or catheter insertion or perianal fissure in granulocytopenic patients); *Corynebacterium striatum* (infection of exit sites of central venous catheters); *Corynebacterium urealyticum* (immunosuppressed); *Actinobacillus actinomycetemcomitans* (soft tissue abscess; may be associated with infection with *Actinomyces*); *Moraxella* (rare); *Sarcina* (rare); *Salmonella* (in renal transplant recipients); *Bacillus cereus* (principal cause of traumatic wound infections in tropics); *Streptococcus pneumoniae* (associated with connective tissue disease); *Haemophilus influenzae* (soft tissue abscesses; 45% of nonbacteremic *Haemophilus influenzae* infections in older children and adults); *Capnocytophaga* (granulocytopenics); *Selenomonas sputigena* (in alcoholics); *Desulphovibrio desulfuricans; Candida albicans* (sternal in coronary artery bypass grafting); *Pseudallescheria boydii* (cancer patients); *Trichosporon*, *Fusarium* and *Geotrichum* (mainly disseminated infections in cancer patients); *Aspergillus*, *Alternaria*

Diagnosis: in severe sepsis, organ dysfunction, hypoperfusion or hypotension, fever, tachycardia, tachypnea and elevated white cell count may be present; micro and culture of wound swab, aspirate, body fluids, blood (repeat if negative); serology, counterimmunoelectrophoresis of serum; immunodiffusion, latex agglutination, ELISA (*Bacteroides fragilis* sensitivity 81%, specificity 95%; *Staphylococcus aureus* teichoic acid), radioimmunoassay (*Bacteroides fragilis* sensitivity 75%, specificity 100%)

Wound Botulism: 66% traumatic, 15% injection site, 11% surgical, 6% unknown site, 4% sinusitis; culture of wound, cyst aspirate, stool; electromyogram (median nerve conduction and F-responses normal, amplitude of evoked muscle-action potential low but increased by repetitive stimulation at 10 Hertzogs by 50%); hypercapnia (pCO_2 = 110)

Treatment: in severe sepsis, i.v. fluids if hypotensive or hypoperfusion, vasopressors if hypotension not corrected by i.v. fluids, intubate and ventilate as necessary, control source of sepsis where possible, maintain adequate glycemic control; where not contraindicated, drotrecogin alpha (activated) (recombinant human activated protein C) reduces mortality by 20%

Organism Not Known: as for **Muscular, Skeletal and Soft Tissue Trauma** or, if severe, as for **Bacteremia, Septicemia, Septic Shock**

***Streptococcus pyogenes*:** aqueous benzylpenicillin 6-8 MU i.v. daily, procaine benzylpenicillin 1.2-2.4 MU i.m. twice daily, phenoxymethylpenicillin 1-2 g daily orally

***Staphylococcus aureus*:** oxacillin or flucloxacillin 6-12 g i.v. daily in divided doses, cephazolin 3-4 g/d, vancomycin 500 mg every 6 h, dicloxacillin 250-500 mg 4 times a day orally, erythromycin, cephalexin 250-500 mg 4 times a day orally

Enterococci: benzylpenicillin 9-12 MU daily or ampicillin 6-12 g i.v. daily + gentamicin 1 mg/kg 8 hourly

***Mycobacterium*:** debridement, drainage, excision + sulphamethoxazole 1 g orally 8 hourly for 10 w or more; amikacin 500 mg i.v. 12 hourly ± cefoxitin 1.2 g 4-8 hourly; amikacin 300 mg i.v. 12 hourly + doxycycline 100 mg orally 8 hourly

Corynebacterium jeikeium, Corynebacterium urealyticum, Corynebacterium striatum: vancomycin

Chromobacterium violaceum: chloramphenicol

Campylobacter fetus* subsp *fetus: gentamicin

***Salmonella*:** drainage + ampicillin

***Vibrio*:** debridement; doxycycline 100 mg orally or i.v. twice daily + ceftazidime 2 g i.v. 3 times a day or ciprofloxacin 400 mg twice a day for 3 d or gentamicin

***Aeromonas*:** thorough cleaning of wound, topical antiseptics; consider delayed primary closure; surgical drainage + gentamicin

***Pseudomonas*:** ciprofloxacin

Anaerobes: clindamycin

Clostridium botulinum: wound debridement, intensive care, mechanical ventilation when appropriate, antitoxin; tetracycline, metronidazole, chloramphenicol, penicillin

***Bacillus cereus*:**

Mild: flucloxacillin 50 mg (< 2 y: ¼ dose; 2-10 y: ½ dose) orally 6 hourly

Severe: clindamycin 450 mg orally 6 hourly (child: 20 mg/kg daily in equally divided doses)

***Candida*:** ketoconazole 200-400 mg orally daily, fluconazole 50-100 mg orally daily

***Aspergillus*:** amphotericin B; radical debridement essential for management

***Alternaria*:** resection; itraconazole

Fusarium:

Non-neutropenic: itraconazole 200 mg twice daily orally

Neutropenic: amphotericin B 1.0 – 1.5 mg/kg daily, liposomal amphotericin B 5 – 15 mg/kg daily

Methicillin Resistant *Staphylococcus aureus* Control: povidone iodine gauze pads, application of 2% mupirocin calcium ointment to nares of carriers twice daily for 5 d or to wounds daily for 2 w, showering and shampooing with triclosan 2% liquid soap 12 hourly, shortening period of perioperative antibiotic cover, routine postoperative perineal swabs, wearing masks while tending infected patients

Cellulitis, Fasciitis, Gangrene, Myonecrosis, Myositis, Pyomyositis: 0.7% of new episodes of illness in UK; 0.5% of ambulatory care visits in USA; cellulitis = painful, erythematous infection of deep skin with poorly demarcated borders

Agents: *Streptococcus pyogenes* (may be gangrenous or pyomyositis in diabetics; also perianal in young children), *Staphylococcus aureus* (> 90% of pyomyositis—myositis purulenta tropica, staphylococcal pyomyositis, tropical myositis, tropical pyomyositis), *Mycobacterium fortuitum* (emerging pathogen in AIDS), *Mycobacterium smegmatis, Pseudomonas aeruginosa* (punctures or surgical wounds), *Aeromonas hydrophila* (soft tissue trauma associated with water; cellulitis ± bullae, abscesses and crepitant, necrotising, myonecrosis), *Edwardsiella tarda* (similar to *Aeromonas*), *Yersinia enterocolitica* (pyomyositis in diabetics), halophilic *Vibrio* (*Vibrio alginolyticus, Vibrio parahaemolyticus, Vibrio vulnificus), Serratia marcescens* (rare pyomyositis), *Haemophilus influenzae* (usually type b; buccal, associated with otitis media; rare pyomyositis), *Streptococcus milleri*, *Streptococcus canis,* Group C *Streptococcus*, *Streptococcus pneumoniae* (children, chronic illness, alcoholics and i.v. drug users), *Streptococcus agalactiae* (rare; diabetics; including pyomyositis), *Salmonella* (in renal transplant recipients), *Erysipelothrix rhusiopathiae*, *Corynebacterium jeikeium* (biopsy sites in granulocytopenic patients), *Mycoplasma hominis*, *Shewenella putrefaciens* (lower limb), *Edwardsiella tarda* (associated with trauma to mucosal surfaces), *Clostridium perfringens* and other *Clostridium* (*Clostridium fallax, Clostridium novyi, Clostridium oedematiens, Clostridium septicum, Clostridium sporogenes*; gas gangrene, clostridial cellulitis, clostridial myonecrosis (anaerobic myositis, clostridial myositis) from contamination of wounds, incubation period hours; *Clostridium septicum* also spontaneous nontraumatic associated with colon lesions, diabetes, leucopenia), anaerobic streptococci, *Peptococcus*, *Neisseria gonorrhoeae* (rare pyomyositis), *Neisseria mucosa* (rare), *Klebsiella oxytoca* (uncommon pyomyositis), *Legionella pneumophila* (one case associated with pneumonia), *Acinetobacter calcoaceticus, Capnocytophaga canimorsus, Succinimonas amylolytica* (single case of groin cellulitis and abscess), *Stenotrophomonas maltophilia* (associated with neutropenia, prolonged hospitalisation, intensive care unit stay, broad spectrum antibiotic exposure), mixed aerobes and anaerobes, *Mucorales* (uncommon; fulminant necrotising or indolent), *Scedosporium* (post-traumatic), *Bipolaris, Cryptococcus*

Diagnosis: excruciating pain, swelling of tissues, crepitance, bulla formation; Gram stain and culture of swab from deep in necrotic tissue; specimens from sinus tracts or draining wounds may be taken by aspiration by syringe and small plastic catheter introduced as deeply as possible through decontaminated skin orifice, but a specimen obtained at surgery from the depths of the wound or underlying bone lesion is always preferable; curettings and tissue biopsies provide excellent material; Gram stain will frequently be an important clue to nature of infection; blood cultures; Doppler imaging to rule out deep vein thrombosis in absence of visible port of entry or recognisable predisposing factor in elderly

Necrotising Infections: edema > erythema, skin vesicle, subcutaneous gas, absence of lymphadenitis/lymphangitis; later, skin echymoses, anesthesia, fever, hypotension

Anaerobic Cellulitis: will often be suspected clinically because of smell and appearance of wound

Clostridial Cellulitis: production of gas in subcutaneous tissue, resulting in their destruction; some local pain, moderate fever and crepitation common

Clostridial Myonecrosis: local pain in region of wound, toxemia, toxic delirium, edema, production of bullae, tissue necrosis (in that order)

Gas Gangrene: necrosis and production of gas in tissues; gas in soft tissues may be due to *Clostridium*, *Escherichia coli*, *Klebsiella*, *Peptostreptococcus*, *Bacteroides*, *Fusobacterium*, *Streptococcus pyogenes*, mixed facultative and anaerobic bacteria, or noninfectious (eg., trapped air following trauma or surgery)

Streptococcal: extremely rapid spread; patient appears toxic; lymphangitis prominent

Staphylococcal: more indolent, central fluctuance

Pyomyositis: fever, muscle pain; needle aspiration if visible mass; ultrasonography, X-ray, radionuclide bone scintigraphy, gallium scan, MRI

***Haemophilus*:** primarily in children aged 3 mo - 3 y; bluish tinge; frequently facial

***Aeromonas*:** inflammation of connective tissue often resembling β-haemolytic streptococcal cellulitis; occasionally seen as a granulomatous ulcer; rarely hemorrhage, necrosis and liquefaction of soft tissues (muscle), subcutaneous gas formation, muscle fibres separated and lysed (high mortality associated with positive blood culture); usually results from exposure of lesion to fresh water

***Vibrio*:** exposure to marine water; widespread fasciitis and myonecrosis; case-fatality rate 7-33%

Other Gram Negative Bacilli: immunocompromised host

***Erysipelothrix rhusiopathiae*:** summer peak; exposure to fish, shellfish; erysipeloid; joint involvement common

***Mycoplasma hominis*:** postcaesarean and others; culture on A7B or Mycotrim-GU (Hana)

Treatment: surgical incision and drainage of abscesses and surgical debridement of all necrotic tissue + antimicrobial; planned relook 24-48 h

Mild Early: di/flucloxacillin 12.5 mg/kg to 500 mg orally 6 hourly for 7-10 d

Penicillin Hypersensitive (Not Immediate): cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 7-10 d

Immediate Penicillin Hypersensitivity: clindamycin 10 mg/kg to 450 mg orally 8 hourly for 7-10 d

Severe: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly, cephazolin 50 mg/kg to 2 g i.v. 8 hourly

Immediate Penicillin Hypersensitivity: clindamycin 10 mg/kg to 450 mg i.v. or orally 8 hourly, lincomycin 15 mg/kg to 600 mg i.v. 8 hourly, vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

***Streptococcus pyogenes*:**

Severe: benzylpenicillin 30 mg/kg to 600 mg i.v. 4 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 25 mg/kg to 1 g i.v. 8 hourly

Immediate Penicillin Hypersensitivity: clindamycin 10 mg/kg to 450 mg i.v. then 10 mg/kg to 450 mg orally 8 hourly; lincomycin 15 mg/kg to 600 mg i.v. 8 hourly, then clindamycin 10 mg/kg to 450 mg orally 8 hourly; vancomycin 20 mg/kg to 1 g i.v. slowly 12 hourly

Home-based Therapy: cephalzolin 2 g i.v. 12 hourly for 4-7 d; cephalzolin 2 g i.v. daily for 4-7 d + probenecid 1 g orally daily for 4-7 d

Less Severe: procaine penicillin 50 mg/kg to 1.5 g daily, phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly for 7 d

Penicillin Hypersensitive: clindamycin 10 mg/kg to 450 mg orally 8 hourly

***Staphylococcus aureus*:**

Less Severe: di(flu)cloxacillin 25 mg/kg to 500 mg orally 6 hourly

Penicillin Hypersensitive: clindamycin 10 mg/kg to 450 mg orally 8 hour

Severe: di/flucloxacillin 50 mg/kg to maximum 2 g i.v. 6 hourly

Penicillin Hypersensitive, Home-based Therapy: as for *Streptococcus pyogenes*

Methicillin Resistant *Staphylococcus aureus*:

Mild: fusidic acid 500 mg (5-12 y: 250 mg) orally 8 hourly + rifampicin 600 mg orally twice daily (not pregnant; child: 1 mo - 1 y: 10 mg/kg daily; > 1 y: 20 mg/kg to maximum 120 mg daily)

Severe: vancomycin 500 mg i.v. 6 hourly over 60 min for 4 w (child: 44 mg/kg i.v. daily in divided doses) + gentamicin 1 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly for at least 2 w or rifampicin as above

***Clostridium*:** complete surgical wound debridement of necrotic tissue; hyperbaric oxygen if severe; benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly; if immediate penicillin hypersensitivity, metronidazole 12.5 mg/kg to 500 mg i.v. 8 hourly

Other Anaerobes: chloramphenicol 500 mg orally 6 hourly (child > 2 w: 50 mg/kg daily orally in 4 divided doses; premature, newborn and those with immature metabolism: 25 mg/kg daily in 4 divided doses), metronidazole as for ***Clostridium***

Mycobacterium fortuitum: 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

Mycobacterium smegmatis: extensive skin debridement followed by skin grafting

***Haemophilus influenzae*:**

Severe: cefotaxime 500 mg i.v. 6 hourly (child: 30-50 mg/kg i.v. 6-8 hourly), chloramphenicol as for

Other Anaerobes

Less Severe: amoxycillin-clavulanate 40/10 mg/kg/d to maximum 1.5/0.375 g in 3 divided doses

***Aeromonas hydrophila, Edwardsiella tarda*:** ciprofloxacin, aminoglycoside, third generation cephalosporin

***Vibrio*:** doxycycline 100 mg orally or i.v. twice daily + ceftazidime 2 g i.v. 3 times a day or ciprofloxacin 400 mg twice a day for 3 d or gentamicin

***Mycoplasma hominis*:** doxycycline

Stenotrophomonas maltophilia: resection + cotrimoxazole + ticarcillin-clavulanate + aztreonam

Other Aerobic Gram Negatives: ticarcillin + gentamicin

Erysipelothrix rhusiopathiae: penicillin

Fungi: amphotericin B 0.75mg/kg/d

Prophylaxis (Recurrent *Streptococcus pyogenes* Cellulitis): phenoxymethylpenicillin 250 mg orally twice daily for up to 6 mo

Necrotising Fasciitis: incidence in adults 0.4/100,000, in children 0.08/100,000; mortality rates up to 73%; diabetes mellitus, immunosuppressive medications and AIDS predispose

Type I (Progressive Synergistic Bacterial Gangrene)

Agents: classically microaerophilic streptococci + *Staphylococcus aureus* (Meleney's synergistic gangrene) but also applied to situations involving other streptococci (30% of isolates), *Staphylococcus aureus* (gives a chronic condition), Gram negative bacilli (especially *Escherichia coli*, *Pseudomonas*, *Shigella, Enterobacter, Proteus, Serratia*), *Enterococcus faecalis* and various anaerobes (particularly *Bacteroides, Peptostreptococcus, Clostridium, Peptococcus*); may develop as a complication of foot and leg sores in diabetics, occasionally in other situations; Fournier's gangrene is necrotising fasciitis of scrotum rapidly progressing to penis and is caused by *Peptostreptococcus* in association with *Proteus*, *Escherichia coli*, *Staphylococcus aureus*, β-haemolytic streptococci (rarely *Streptococcus agalactiae* associated with diabetes) and various anaerobes; may follow use of nonsteroidal antiinflammatory drugs in treating inflammatory cutaneous lesions

Type II (Hemolytic Streptococcal Gangrene): prior injury (penetrating injuries, cuts, burns, blunt trauma, muscle strain, surgical incisions, irradiation, cancer, diabetes, infection on trunk, alcoholism, HIV infection, cardiovascular and pulmonary disease, puerperium predisposing factors; also associated with use of nonsteroidal antiinflammatory drugs in varicella; 74% mortality

Agents: *Streptococcus pyogenes*, occasionally in combination with *Staphylococcus aureus*

Diagnosis: localised pain ± swelling, tenderness or erythema in 87%, gastrointestinal complaints (nausea, vomiting, diarrhoea) in 53%, influenza-like symptoms (aches, chills, fever) in 47%; culture of swab or biopsy from deep in wound; blood cultures; C reactive protein ≥ 16 mg/dL (positive predictive value 44%, negative predictive value 99%), creatine kinase ≥ 600 U/L (positive predictive value 58%, negative predictive value 95%); MRI (94% accuracy) or CT scan (exudates extending along fascial planes); frozen section; 'finger test' pathognomonic

Treatment: operative removal of devitalised tissue; meropenem 25 mg/kg to 1 g i.v. 8 hourly + clindamycin 15 mg/kg to 600 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly; supportive care in ICU critical

Streptococcus pyogenes: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly + clindamycin 15 mg/kg to 600 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly + normal immunoglobulin 0.4-2 g/kg i.v. for 1 or 2 doses during first 72 h; debridement; hyperbaric oxygen

Penicillin Hypersensitive: substitute cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 50 mg/kg to 2 g i.v. 8 hourly for benzylpenicillin

Pseudomonas aeruginosa: extensive debridement and resection; combination antipseudomonas antimicrobial therapy; leucocyte transfusions or colony-stimulating factors

Polymicrobial: meropenem 25 mg/kg to 1 g i.v. 8 hourly

Lymphocutaneous Syndrome

Agents: *Sporothrix schenckii* (most common), *Nocardia brasiliensis* (very common), *Mycobacterium marinum* (very common), *Leishmania braziliensis* (very common in endemic areas), *Leishmania tropica* (common in endemic areas), *Coccidioides immitis* (common), *Francisella tularensis* (common), *Mycobacterium chelonaei* (common), less frequent *Ajelloomyces dermatitidis, Cryptococcus neoformans, Fusarium, Histoplasma capsulatum, Scedosporium apiospermum, Scopulariopsis, Nocardia asteroides, Nocardia otitidiscaviarum, Nocardia transvalensis, Staphylococcus aureus, Streptococcus pyogenes, Mycobacterium avium-intracellulare, Mycobacterium flavescens, Mycobacterium fortuitum* (emerging pathogen in AIDS), *Mycobacterium kansasii, Mycobacterium tuberculosis, Leishmania major, cowpox virus*, *simplexvirus*

Diagnosis: biopsy and culture of skin lesion, lymph node

Treatment:

Scedosporium apiospermum: ketoconazole, fluconazole, flucytosine

Sporothrix schenckii: itraconazole

Other Fungi: amphotericin B 0.75 mg/kg i.v daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 14 d

Francisella tularensis: streptomycin, tetracycline

Staphylococcus aureus: cloxacillin, flucloxacillin, cephalothin

Streptococcus pyogenes: penicillin, erythromycin

Nocardia, Mycobacterium chelonae, Mycobacterium fortuitum: 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

***Mycobacterium avium-intracellulare*:** ethambutol 15 mg/kg orally daily or 25 mg/kg orally 3 times weekly (not < 6 y) + clarithromycin 12.5 mg/g to 500 mg orally 12 hourly daily or 3 times weekly or azithromycin 10 mg/kg to 500 mg orally daily or 10 mg/kg to 600 mg orally 3 times weekly + rifampicin 10 mg/kg to 600 mg orally daily or 3 times weekly or rifabutin 5 mg/kg to 300 mg orally daily

Mycobacterium kansasii: isoniazid 10 mg/kg to 300 mg orally daily + rifampicin 10 mg/kg to 600 mg orally twice daily + ethambutol 15 mg/kg orally (not < 6 y) daily for 18 mo and 12 mo negative sputum cultures

Mycobacterium marinum: clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly, cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly, doxycycline 2.5 mg/kg to 100 mg orally (not < 8 y) 12 hourly

Severe or Unresponsive: clarithromycin + rifampicin or ethambutol

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Leishmania: sodium stibogluconate

***Simplexvirus*:** famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

Prophylaxis (*Mycobacterium avium* Complex in HIV/AIDS, CD4 Count < 50/μL): azithromycin 1.2 g orally weekly, clarithromycin 500 mg orally 12 hourly, rifabutin 300 mg orally daily

RHABDOMYOLYSIS: 5% due to infectious causes

Agents: influenza virus, human parainfluenza virus, coxsackievirus, echovirus, *Epstein-Barr virus*, *hepatitis B virus*, *simplexvirus*, adenovirus, *Clostridium*, *Streptococcus pneumoniae*, other *Streptococcus*, *Staphylococcus aureus*, *Salmonella typhi, Shigella sonnei, Shigella flexneri, Legionella, Haemophilus parainfluenzae, Escherichia coli, Vibrio vulnificus, Klebsiella pneumoniae, Leptospira*

Diagnosis: culture of muscle biopsy, blood; test of urine for myoglobin; serology; raised serum aldolase, serum creatine kinase

Treatment: ticarcillin + tobramycin

SARCOCYSTOSIS

Agent: *Sarcocystis suihominis*

Diagnosis: histology of cysts in muscle

Treatment: none satisfactory

SYMMETRICAL PERIPHERAL GANGRENE: complication of septicemia

Agents: usually Gram negative bacilli; also staphylococci and streptococci

Diagnosis: culture of blood and urine

Treatment: dependent on isolate

NASAL SEPTAL ABSCESS

Agents: *Staphylococcus aureus*, *Streptococcus pneumoniae*, β-haemolytic streptococci, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Escherichia coli*

Diagnosis: culture of aspirate

Treatment: cephalexin + gentamicin + aspiration, drainage and nasal packing

ISCHIORECTAL ABSCESS

Agents: *Clostridium*, *Bacteroides*, *Staphylococcus aureus* (coliforms and enterococci which may be isolated are not significant)

Diagnosis: culture of swab from deep in abscess

Treatment: penicillin, cephalosporin or erythromycin + metronidazole

Perianal and Perirectal Abscess and Cellulitis in Patients with Malignant Disease

Agents: *Escherichia coli*, Group D *Streptococcus*, *Bacteroides fragilis*, *Clostridium*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* (55% of patients with acute leukemia; > 50% case-fatality rate in these cases), *Proteus mirabilis, Citrobacter freundii, Staphylococcus aureus, Enterobacter cloacae, Candida albicans*

Diagnosis: swab culture

Treatment: ceftazidime + clindamycin, piperacillin + tobramycin + clindamycin; + vancomycin if progression; + surgery if inadequate response

Perianal Cellulitis in Young Children

Agent: *Streptococcus pyogenes*

Diagnosis: culture of anal swab

Treatment: phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly for 7 d

Psoas Abscess: ≈ 12 reported cases/y worldwide; predisposing conditions diabetes, immunosuppression, renal failure

Agents: *Staphylococcus aureus* (80% of primary), *Pseudomonas aeruginosa, Haemophilus aphrophilus, Proteus mirabilis, Escherichia coli, Streptococcus viridans*, β-haemolytic streptococci, *Enterobacter, Salmonella enteritidis, Enterococcus*, *Serratia marcescens, Bacteroides fragilis, Mycobacterium tuberculosis* (uncommon), *Mycobacterium kansasii, Mycobacterium xenopi, Pasteurella multocida*, *Salmonella typhi* (rare), *Candida tropicalis, Torulopsis glabrata*

Diagnosis: computerised tomography; Gram stain and culture of aspirate; culture of blood and urine

Treatment: surgical drainage +:

***Staphylococcus aureus*:** cloxacillin

Streptococci, *Pasteurella multocida*: penicillin

***Serratia marcescens*:** gentamicin

Anaerobes: metronidazole

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

***Salmonella typhi*:** ciprofloxacin 1.5 g/d orally

***Candida*, *Torulopsis*:** amphotericin B

Organism Not Known: cloxacillin + gentamicin + clindamycin

Intraabdominal Abscess: 12% from pancreatitis, 10-20% from appendicitis, 10% from genitourinary tract, 8% from biliary tract, 7% from diverticulitis, 3% from trauma, 3% from perforating tumours, 2% from peptic ulcer, 2% from leaking suture line, 15-30% from miscellaneous sources, 10% from unknown source

Agents: 80-95% *Bacteroides fragilis*, 80-95% *Escherichia coli*, 60% *Enterococcus*, 50% anaerobic streptococci, 50% *Clostridium*, 40% *Fusobacterium*, 38% *Proteus*, *Eikenella corrodens*, other *Bacteroides*, *Prevotella, Desulfovibrio desulfuricans*

Diagnosis: fever in 82%, abnormal chest film in 61%, abdominal pain in 38%, persistent drainage in 18%, abnormal plain film of abdomen in 14%, chest dullness in 12%, abdominal mass by palpation in 7%; liver-lung scan (98% accurate), CT scan (98% accurate), ultrasound (96% accurate), gallium scan (82% accurate); culture of aspirate or surgical specimen

Treatment: clindamycin, chloramphenicol

Perinephric abscess

Agents: *Staphylococcus* (36% of cases in renal transplant recipients), aerobic Gram negative bacilli (32% of cases in renal transplant recipients), anaerobes (28% of cases in renal transplant recipients), *Candida albicans* (4% of cases in renal transplant recipients), *Mycobacterium intracellulare*

Diagnosis: fever, abdominal tenderness; computed tomography, intravenous pyelogram, cystogram; culture of material obtained by surgery or percutaneous drainage

Treatment: surgical drainage + appropriate antimicrobials

Pelvic Abscess, Pelvic Inflammatory Disease, Parametritis: 62% salpingitis, 22% normal findings, 5% ovarian cysts, 4% ectopic pregnancy, 3% appendicitis, 1% endometriosis; important cause of ectopic pregnancy, sterility and tuboovarian abscess; increasing importance in Australia and other developed nations; vaginal douching a risk factor

Agents: *Neisseria gonorrhoeae*, *Chlamydia trachomatis* (1/4 – ½ of the million recognised cases in USA each year), *Bacteroides*, anaerobic Gram positive cocci, *Escherichia coli*, *Actinomyces israelii* (almost exclusively associated with use of IUD), *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Haemophilus influenzae* (IUD related and maternal), *Streptococcus pyogenes*, *Streptococcus milleri*, *Streptococcus pneumoniae* (IUD, recent birth, gynecologic surgery), *Clostridium perfringens, Candida* (associated with suture, IUD)

Diagnosis: diffuse pelvic (uterine/adnexal, cervical motion) tenderness associated with pelvic pain and abnormal cervical or vaginal mucopurulent discharge, oral temperature > 38.3°C, leucocytes on saline microscopy of vaginal secretions, elevated erythrocyte sedimentation rate, elevated C-reactive protein; increased frequency in patients with IUDs; endometrial biopsy with histopathologic evidence of endometriosis; transvaginal sonography or magnetic resonance imaging showing thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex; laparoscopy; Gram stain and culture of swab or pus; direct immunofluorescence on cervical smears (*Chlamydia*, *Actinomyces israelii*)

Treatment: hospitalise if surgical emergencies cannot be excluded, the patient is pregnant, the patient does not respond clinically to oral antimicrobial therapy, the patient is unable to follow or tolerate an outpatient oral regimen, the patient has severe illness, nausea and vomiting or high fever, or the patient has a tubo-ovarian abscess

Likely to be Sexually Acquired:

Mild to Moderate: azithromycin 1 g orally as single dose weekly for 2 w + ceftriaxone 250 mg i.m. or i.v. as single dose + metronidazole 400 mg orally 12 hourly for 14 d or tinidazole 500 mg orally daily for 14 d

Severe: doxycycline 100 mg orally or i.v. 12 hourly + cefoxitin 2 g i.v. 8 hourly, doxycycline 100 mg orally or i.v. 12 hourly + metronidazole 500 mg i.v. 12 hourly + ceftriaxone 1 g i.v. daily or cefotaxime 1 g i.v. 8 hourly

Penicillin Hypersensitive: gentamicin 4-6 mg/kg (adjust dose for renal function) i.v. daily + clindamycin 600 mg i.v. 8 hourly or lincomycin 600 mg i.v. 8 hourly

Treatment for Sexual Partners: doxycycline 100 mg orally twice daily for 7 d, tetracycline 500 mg 6 hourly for 7 d, erythromycin 500 mg 6 hourly for 7 d

Mild to Moderate Infection, Not Sexually Acquired: remove any IUD or retained products of conception as soon as possible; amoxycillin-clavulanate 875/125 mg orally 12 hourly + doxycycline 100 mg orally 12 hourly for 14 d

Pregnant or Breastfeeding: substitute roxithromycin 300 mg orally daily for 14 d for doxycycline

Related to Trauma or Pregnancy: amoxy/ampicillin 2 g i.v. 6 hourly + metronidazole 500 mg i.v. infused over 20 min 12 hourly or 1 g rectally 8 hourly + gentamicin 4-6 mg/kg i.v 8 daily (adjust for renal function)

Streptococci, *Clostridium perfringens*: benzylpenicillin 2.4 g i.v. 4 hourly

***Candida albicans*:** amphotericin B

PERITONITIS: primary; secondary due to obstruction, infarction, perforation, neoplasm, foreign body, inflammatory bowel disease; spontaneous in patients with ascites due to cirrhosis of liver or nephrotic syndrome; during peritoneal dialysis

Agents: coliforms (primary, secondary, spontaneous; *Klebsiella* 1-6 % of infections in continuous ambulatory peritoneal dialysis, *Escherichia coli* 0-15% of infections in continuous ambulatory peritoneal dialysis; *Enterobacter cloacae*, *Citrobacter freundii*, infrequently *Kluyvera ascorbata*), anaerobes (primary and secondary, < 5% of infections in continuous ambulatory peritoneal dialysis; *Bacteroides*, *Prevotella,* Gram positive cocci, *Clostridium perfringens*, *Bifidobacterium*, *Eubacterium*), *Streptococcus agalactiae* (primary and secondary), *Streptococcus pneumoniae* (primary and spontaneous), *Streptococcus pyogenes* (primary and secondary), *Enterococcus* (primary and secondary and 2-11% of infections in continuous ambulatory peritoneal dialysis), *Streptococcus milleri* (primary and secondary), *Streptococcus viridans* (5-21% of infections in continuous ambulatory peritoneal dialysis), *Staphylococcus aureus* (primary and 9-24% of infections in continuous ambulatory peritoneal dialysis), coagulase negative *Staphylococcus* (primary and adherent strains in 32-45% of infections in continuous ambulatory peritoneal dialysis), *Neisseria gonorrhoeae* (primary; gonococcal perihepatitis (Fitz-Hugh syndrome, Fitz-Hugh and Curtis syndrome, Fitz-Hugh-Curtis syndrome, gonococcic perihepatitis, gonococcic peritonitis of the upper abdomen, Stojano subcostal syndrome, Stojano syndrome, subcostal syndrome); upper abdominal peritonitis arising by extension of gonococcal salpingitis, with string-like adhesions between liver and abdominal wall), *Chlamydia trachomatis*, *Actinomyces israelii*, *Mycoplasma hominis*, *Pseudomonas* (primary and secondary and in 0-8% of infections in peritoneal dialysis), *Mycobacterium tuberculosis* (primary; 0.2% of tuberculosis cases), *Capnocytophaga* (primary and secondary), *Listeria monocytogenes*, *Neisseria meningitidis*, *Aeromonas* (nosocomial), *Haemophilus influenzae* (13% of non-bacteremic invasive *Haemophilus influenzae* infections in older children and adults), *Campylobacter fetus* subsp *fetus*, *Pseudomonas luteola* and *Pseudomonas oryzihabitans* (in continuous ambulatory peritoneal dialysis), *Agrobacterium tumefaciens* (in continuous ambulatory peritoneal dialysis), *Rothia mucilaginosa* (in continuous ambulatory peritoneal dialysis), *Mycobacterium chelonae* and *Mycobacterium fortuitum* (in < 3% of infections in continuous ambulatory peritoneal dialysis; emerging pathogen in AIDS), *Corynebacterium jeikeium* (in continuous ambulatory peritoneal dialysis), *Sphingobacterium multivorum* (spontaneous), *Alcaligenes xylosoxydans xylosoxydans, Bordetella bronchiseptica, Pasteurella multocida* (infant appendicial), *Nocardia* (infrequent in continuous ambulatory peritoneal dialysis), *Bacteroides fragilis* in continuous ambulatory peritoneal dialysis complicating colon cancer, fungi (in ≤ 5% of infections in continuous ambulatory peritoneal dialysis; 42% *Candida albicans*, 14% *Candida tropicalis*, 8% *Candida parapsilosis, 3% Candida guilliermondii,* 2% *Candida glabrata*, 1% *Candida krusei*, 6% other *Candida*, 7% *Fusarium, 3% Rhodotorula rubra*, 2% *Bipolaris spicifera,* 1% *Mucor*, 1% *Aspergillus flavus,* 1% *Aspergillus fumigatus,* 1% *Dreschslera*, 1% *Trichoderma longibrachiatum* and *Trichoderma viride*, 1% *Exophiala jeanselmei*, 1% *Cephalosporium*, rare *Alternaria*, *Curvularia*, *Trichosporon beigelii, Cochliobolus australiensis, Bipolaris spicifera; Cryptococcus* up to 6% and *Coccidoides* up to 4% in some series) , amoebae (secondary), *Strongyloides* (secondary), *Balantidium coli* (very rare)

Diagnosis: culture of swab or pus; counterimmunoelectrophoresis of serum, peritoneal fluid; urinalysis reagent strip test for leucocyte esterase on ascitic fluid (> 3 = +ve gives sensitivity 89%, specificity 99%, positive predictive value 98%; > 2 = +ve gives sensitivity 96%, specificity 89%, negative predictive value 99%; direct immunofluorescence of cervical smears (*Chlamydia*, *Actinomyces israelii*); serum lipase often increased

Gonococcal Perihepatitis: right upper quadrant pain and tenderness

Tuberculous: laparoscopy

Continuous Ambulatory Peritoneal Dialysis: cloudy dialysis effluent in 95% of cases, abdominal pain in 78%, abdominal tenderness in 76%; peritoneal dialysis fluid white cell count (90-2880 cells/mL with 56-99% polymorphonuclears in fungal peritonitis) and culture as for blood culture (Isolator, Bactec, BacT/Alert Aerobic FAN)

Treatment:

Suspected Associated with PID: doxycycline + cefoxitin 2 g i.v. 8 hourly

Suspected Bowel Origin: amoxy(ampi)cillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. as single daily dose (adjust dose for renal function) + metronidazole 12.5 mg/kg to 500 mg i.v. infused over 20 min 12 hourly

Gentamicin Contraindicated: piperacillin-tazobactam 100/12.5 mg/kg to 4/0.5 g i.v. 8 hourly, ticarcillin-clavulanate 50/1.7 mg/kg to 3/0.1 g i.v. 6 hourly

Penicillin Hypersensitive (Not Immediate): metronidazole 12.5 mg/kg to 500 mg i.v. 12 hourly + cefotaxime 25 mg/kg to 1 g i.v. 8 hourly or ceftriaxone 25 mg/kg to 1 g i.v. daily

Immediate Penicillin Hypersensitive: vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly) + gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. as single daily dose (adjust dose for renal function) + metronidazole 12.5 mg/kg to 500 mg i.v. infused over 20 min 12 hourly

Spontaneous: ceftriaxone 25 mg/kg to 1 g i.v. once daily or cefotaxime 25mg/kg to 1 g i.v. 8 hourly or ticarcillin + clavulanate 50 + 1.7 mg/kg to 3 + 0.1 g i.v. 6 hourly + (if receiving cotrimoxazole or norfloxacin prophylaxis or enterococcal infection likely) amoxy/ampicillin 25 mg/kg to 1 g i.v. 6 hourly

Continuous Ambulatory Peritoneal Dialysis: flush 2 X 1 L exchanges of dialysate

Gram Positive Organisms Seen in Dialysate: cephalothin 15 mg/kg added to 1 bag/d (intermittent) or 500 mg/L initially then 125 mg/L (continuous with each bag exchange), cephazolin 15 mg/kg added to 1 bag/d (intermittent) or 500 mg/L initially then 125 mg/L (continuous with each bag exchange), vancomycin 25 mg/L in each bag of dialysate or 50 mg/kg to 2 g i.p. as single dose, repeated after 7 d

Gram Negative Bacilli Seen in Dialysate: gentamicin 4-8 mg/L to each bag of dialysate to maximum 40 mg/d in dialysate for 10-20 d or 50 mg i.p. as single daily dose for 10-21 d

Diverticular Disease or Bowel Involvement Suspected: as above + metronidazole 400 mg orally or 500 mg i.v. 12 hourly

Streptococci and *Neisseria gonorrhoeae*: penicillin 100,000 U/kg/d

Staphylococci:

Primary: penicillinase-resistant penicillin 150-200 mg/kg/d

Peritoneal Dialysis: as for **Continuous Ambulatory Peritoneal Dialysis**

Mixed Aerobes and Anaerobes: gentamicin or tobramycin 5-7 mg/kg/d + clindamycin 30 mg/kg/d or chloramphenicol 50-100 mg/kg/d

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Mycobacterium chelonae, Mycobacterium fortuitum: 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

***Rothia mucilaginosa*:** vancomycin

***Capnocytophaga*, *Listeria monocytogenes*:** ampicillin

Fungi: amphotericin B total dose of 2-10 mg/kg X 7-14 d i.v. + 1.5-2 mg/L in dialysate up to a total dose of 1500 mg ± flucytosine, followed by catheter removal (essential for management); *Trichoderma* resistant to most agents

Prophylaxis (Spontaneous Bacterial in Patients with Ascites and Gastrointestinal Bleeding or Ascitiic Protein Concentration < 10 g/L or With Previous History): cotrimoxazole 4/20 mg/kg to 160/800 mg orally daily or, if contraindicated or previous failure, norfloxacin 10 mg/kg to 400 mg orally daily

CERVICAL FASCIAL SPACE INFECTIONS: submandibular (Ludwig's angina; follows infection of second or third mandibular tooth in 70-85% of cases; potentially life-threatening), lateral pharyngeal (postanginal sepsis (necrobacillosis, Lemierre's disease); dental infections, rarely parotitis, otitis, mastoiditis), retropharyngeal, danger and prevertebral spaces (suppurative adenitis following upper respiratory tract infection, traumatic penetration, odontogenic)

Agents: *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Bacteroides*, *Peptostreptococcus*, *Fusobacterium necrophorum, Eikenella corrodens, Arcanobacterium haemolyticum*

Diagnosis: ultrasonography, computerised axial tomography; blood cultures; serum alkaline phosphatase 81-330 IU/mL, serum bilirubin total 0.4-10.8 mg/dL, direct 0-7.5 mg/dL, serum gamma-glutamyl transferase 106-258 U/mL, serum glutamic-oxaloacetic acid transaminase 93-192 U/mL, serum glutamic-pyruvic acid transaminase 16-66 U/mL, serum lactic dehydrogenase 212-393 IU/mL, white cell count 7200-31,400/μL

Submandibular: pain, minimal trismus, swelling of mouth floor and submylohyoid region, dysphagia and dyspnoea present if bilateral involvement

Anterior Lateral Pharyngeal: severe pain, prominent trismus, swelling of anterior lateral pharynx and angle of jaw, dysphagia, occasional dyspnoea; followed by bacteremia and metastatic abscesses in necrobacillosis

Posterior Lateral Pharyngeal: minimal pain, minimal trismus, swelling of posterior lateral pharynx (hidden), dysphagia and severe dyspnoea

Retropharyngeal/Danger: pain, minimal trismus, swelling of posterior pharynx, dysphagia and dyspnoea

Treatment: airway management, heparin + surgical drainage or computed tomography-guided needle aspiration +: metronidazole 12.5 mg/kg to 500 mg i.v. 12 hourly + benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 6 hourly; with clinical improvement, change to metronidazole 10 mg/kg to 400 mg orally 12 hourly + phenoxymethylpenicillin 10 mg/kg to 500 mg orally 6 hourly or amoxycillin 10 mg/kg to 500 mg orally 8 hourly, or amoxycillin + clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 12 hourly alone, for further 5 d

Penicillin Hypersensitive: clindamycin 10 mg/kg to 450 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly then clindamycin 10 mg/kg to 450 mg orally 8 hourly for total 10 d

CRANIAL PARAMENINGEAL DEEP FASCIAL SPACE INFECTIONS: direct extension from sinusitis, otitis media, mastoiditis, petrous osteomyelitis; also odontogenic and following cranial surgery

Agents: *Bacteroides*, *Peptostreptococcus*, *Veillonella*, *Actinomyces*, *Fusobacterium*, microaerophilic *Streptococcus*; enteric Gram negative bacilli, *Pseudomonas aeruginosa* and *Staphylococcus aureus* in immunocompromised and otogenic infection

Diagnosis: ultrasonography, computerised axial tomography, blood cultures

Treatment:

Normal Patient:

Otogenic: benzylpenicillin 2-4 MU i.v. every 4-6 h or ciprofloxacin 0.4 g i.v. every 12 h + metronidazole 0.5 g i.v. every 6 h or chloramphenicol 0.5 g i.v. every 6 h

Rhinogenic/Odontogenic: benzylpenicillin 2-4 MU i.v. every 4-6 h + metronidazole 0.5 g i.v. every 6 h or chloramphenicol 0.5 g i.v. every 6 h

Following Cranial Surgery: flucloxacillin 1.5 g i.v. every 4-6 h + tobramycin 2 mg/kg i.v. every 8 h or ciprofloxacin 0.4 g i.v. every 12 h

Immunocompromised:

Otogenic/Rhinogenic/Odontogenic: cefotaxime 2 g i.v. every 6 h, ceftizoxime 4 g i.v. every 8 hours, imipenem 500 mg i.v. every 6 h

Following Cranial Surgery: vancomycin 0.5 g i.v. every 6 hours + cefotaxime, ceftizoxime or imipenem

MASTITIS AND BREAST ABSCESS

Agents: usually *Staphylococcus aureus* in acute; most commonly coagulase negative *Staphylococcus*, *Peptostreptococcus*, *Propionibacterium*, *Eubacterium* and *Bacteroides* in chronic; also α-haemolytic streptococci, *Streptococcus pyogenes*, microaerophilic streptococci, *Proteus*, *Escherichia coli, Prevotella disiens, Corynebacterium minutissimum* (1 case; recurrent) and others

Diagnosis: culture of pus swab, milk

Treatment:

Acute: di(flu)cloxacillin 500 mg orally 6 hourly for at least 5 d; cephalexin 500 mg orally 6 hourly for at least 5 d if penicillin hypersensitive (not immediate); clindamycin 400 mg orally 8 hourly for at least 5 d if immediate penicillin hypersensitivity; if severe cellulitis, di(flu)cloxacillin 2 g i.v. 6 hourly or cephalothin 2 g i.v. 6 hourly or cephazolin 2 g i.v. 8 hourly if penicillin hypersensitive (not immediate) or clindamycin 450 mg i.v. or orally 8 hourly or lincomycin 600 mg i.v. 8 hourly or vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g 12 hourly (monitor blood levels and adjust dose accordingly); prevention of milk stasis by suckling or expression manually or by pump; if no improvement in 2-3 d, surgical drainage

Chronic: amoxycillin-clavulanate or ampicillin-sulbactam; drainage with duct excision in advanced chronic

MYCETOMA (MADURA FOOT, MADUROMYCOSIS): 60% actinomycetoma (actinomycotic mycetoma) due to bacteria, 40% eumycetoma due to fungi; chronic progressive disease of skin, subcutaneous tissue and bone, usually arising secondary to trauma

Agents: *Nocardia asteroides, Nocardia brasiliensis, Nocardia caviae, Actinomadura madurae, Actinomadura pelletieri, Streptomyces somaliensis, Streptomyces paraguayensis, Actinomyces israelii, Pseudallescheria boydii, Aspergillus nidulans, Fusarium falciforme, Streptomyces recifensis, Neotestudina rosatii, Exophiala jeanselmei, Madurella mycetomatis, Streptomyces pseudoechinosporeus, Curvularia geniculata, Curvularia lunata, Leptosphaeria senegalensis, Pyrenochaeta romeroi*

Diagnosis: swelling and formation of granulomata, abscesses and deep sinuses; most characteristic feature presence of granules; brown to black grains produced by *Exophiala, Madurella, Curvularia, Leptosphaeria, Pyrenochaeta, Streptomyces paraguayensis*, yellow to brownish by *Streptomyces somaliensis*, bright red by *Actinomadura pelletieri*, white to yellowish by others; Gram stain, modified Ziehl-Neelsen stain and KOH preparation, bacterial and fungal culture (BHI and Sabaroud's at 30°C) of pus, curettings, biopsy or grains from draining sinuses; X-rays of affected part, and radionuclide scanning if negative, for underlying bone involvement

Treatment: surgery +:

***Actinomyces*:** penicillin

Nocardiforms*:* i.v. cotrimoxazole or dapsone + amikacin or streptomycin, penicillin, tetracycline, rifampicin

Fungi: may show some response to amphotericin B, flucytosine, ketoconazole, miconazole, itraconazole, thiabendazole

BACTEREMIA, SEPTICEMIA, SEPTIC SHOCK: 1.8-13/1000 (13-15/1000 age > 60 y) hospital admissions; case-fatality rate 5-50% (5% in < 60 y, 22% in > 60 y); community acquired: 24% from respiratory tract, 23% urinary tract, 11% meningitis, 6% gastrointestinal tract, 6% cellulitis and decubitus, 3% bone and joint, 2% abdomen, 2% shunt; nosocomial: 18% from urinary tract, 17% hyperalimentation of intravenous site, 12% respiratory tract, 11% surgical wound, 8% abdomen, 8% gastrointestinal tract, 5% cellulitis and decubitus, 1% shunts; transient bacteremia characteristic of dental treatment; overflow bacteremia may be seen in patients with meningococcal meningitis, pneumonia, pyelonephritis; intermittent or constant bacteremia in infective endocarditis; 46% of bacteremic patients in long term care have cardiovascular disease

Agents: *Escherichia coli* (12-29% of total cases, 20-33% of community acquired, 12-18% of nosocomial, 13% of long term care; fifth most common organism in nosocomial infection in cancer patients; 24% of cases in leukemia, lymphoma, solid tumours; common in neutropenics (14%); case-fatality rate 25% in leukemia and lymphoma, 12% in solid tumours, 12% in nosocomial, 13% overall; 98-100% of isolates true infection; 96% clinically significant; 58% hospital acquired; 43-55% from genituourinary tract, 17% abscess, 15-16% unknown, 8-17% bowel, 8-15% hepatobiliary, 6% multiple, 4% wound, 2-11% respiratory; also neonatal), *Staphylococcus aureus* (10-30% of total cases, 9% of community acquired (25% of these associated with arteriosclerotic heart disease), 14% of nosocomial (80% of these associated with intravascular devices), 15% of long term care (5% methicillin resistant); second most common organism in cancer patients; 9% of cases in leukemia and lymphoma, 11% solid tumours; 57% in narcotic addicts (24% methicillin resistant); common in neutropenics (5%); case-fatality rate 14% in leukemia and lymphoma, 22% in solid tumours, 12% in nosocomial, 30% overall; 75-99% of isolates true infection; 94% clinically significant; 60% hospital acquired; 20-33% associated with intravenous catheters, 20-21% unknown, 11-16% from postoperative wounds, 7-29% from respiratory tract, 7% from skin infections, 7% from endocarditis, 7% from multiple, 6% from bone and joint; septicemia (staphylococcal pyaemia), with the presence of large numbers of multiplying staphylococci and of their toxic products in the bloodstream, may take a fulminant course and lead to septicemic adrenal haemorrhage syndrome), coagulase negative *Staphylococcus* (74% *Staphylococcus epidermidis,* 14% *Staphylococcus hominis,* 14% *Staphylococcus haemolyticus*, 6% *Staphylococcus warneri*; 5% of total cases, 3% of community acquired, 15% of nosocomial, 4% of long term care; common in neutropenics (14%; catheter-induced); most common organism in nosocomial infections in cancer patients; 11-37% case-fatality rate in nosocomial (septic shock in 22%), 25% overall; 56-94% of isolates contaminants; 20% significant; 31-68% from intravascular catheter, 19% wound, 16% multiple, 9% gastrointestinal tract, 4% bone and joint, 3-50% genitourinary tract, 3% endocarditis, 3% oropharyngeal, 0-50% CNS), *Streptococcus pneumoniae* (50,000-63,000 cases/y in US; case rate 15-30/100,000 for adults and 50-83/100,000 for ≥ 65 y; 4-8% of total cases, 3% of long term care; all isolates true infection; 96% clinically significant; 81% community acquired; 85-94% from respiratory tract, 9% from meningitis; common in neutropenics; also in neonates; case-fatality rate 20% in adults, 60% in elderly; rare cases of hemorrhage and septic shock in infants; bacteremia without a focus of infection responsible for 70% of invasive pneumococcal disease in children < 2 y), *Klebsiella* (4-8% of total cases, 3% of community acquired, 3% of nosocomial, 1% of neonatal, 9% of long term care; eighth most common organism in nosocomial infections in cancer patients; 11% of cases in leukemia and lymphoma, 10% in solid tumours; common in neutropenics (19%); case-fatality rate 66% in leukemia and lymphoma, 29% in solid tumours, 28% in nosocomial, 27-34% overall; 99-100% of isolates true infection; 93% clinically significant; 80% hospital acquired; 24% multiple, 22% urinary tract, 20% unknown, 19% hepatobiliary, 12% gastrointestinal tract, 7-31% respiratory tract, 3-15% surgical wound, 3% oropharyngeal, 2-15% i.v. catheter), *Salmonella* (4% of community acquired, 2% of nosocomial; in renal transplant recipients and in AIDS; intermediate frequency in neutropenics; case-fatality rate 14% overall, 10% in nosocomial; all isolates true infection; all clinically significant; most common *Salmonella*

choleraesuis, *Salmonella typhi* 1% of community acquired), *Pseudomonas* (3-6% of total cases; case-fatality rate 51%; 99-100% of isolates true infection; 95% clinically significant; 32-33% unknown source, 19% multiple, 18-23% genitourinary tract, 17% wound, 14-43% respiratory tract, 9% gastrointestinal tract, 8% hepatobiliary, 7% intravascular, 2% endocarditis; *Pseudomonas aeruginosa* 3% of community acquired, 12% of nosocomial, 5% of long term care; seventh most common organism in nosocomial infection in cancer patients; common in neutropenics (27%); 15% of cases in leukemia and lymphoma (case-fatality rate 54%); overall case-fatality rate 39%, 31% in nosocomial, 9% in narcotic addicts; 83% hospital acquired; *Pseudomonas alcaligenes* neonatal; other species (*Pseudomonas cepacia, Pseudomonas paucimobilis, Pseudomonas pickettii*) all hospital acquired, 42% from respiratory tract, 15% from genitourinary tract, 12% biliary; uncommon in neutropenics; case-fatality rate 31%; also *Shewanella putrefaciens* in patients with chronic infection of lower extremity or associated with severe underlying debility, liver disease, malignancy; *Burkholderia pseudomallei* common in Southeast Asia in rice farmers or their families, associated with diabetes and renal failure; case-fatality rate 85-95%;), *Streptococcus pyogenes* (common in neutropenics, 0.5% of long term care; also chronic heart disease, malignancy and others; 4% of cases nosocomial; 72% from cutaneous or subcutaneous infections, 28% from i.v. drug abusers; 10% mixed infections) and other β-haemolytic streptococci (3-5% of total cases; 3% of cases in leukemia, lymphoma and solid tumours; 5% in neutropenics; case-fatality rate 20% in leukemia and lymphoma, 33% in solid tumours, 17% overall; 91-97% of isolates true infection; 92% clinically significant; 50% community acquired; 33% genitourinary tract, 10% bone and joint, 9-33% respiratory tract, 8-48% surgical wounds, 8% skin, 5% intravascular, 2-8% bowel, 2% endocarditis, 2% multiple, 2% meningitis; *Streptococcus canis* 0.8% of total cases (from cellulitis or abscess in patients with malignancies; 63% > 75 y; 80% men; 93% from skin or soft tissue infection), *Streptococcus agalactiae* in neonates (46% of cases) and also in hospitalised elderly patients with underlying disease, especially diabetes mellitus (4% of long term care; 19% from pneumonia, 19% from soft tissue infections, 11% from urinary tract infections, 8% from arthritis, 8% from osteomyelitis, 6% from lymphadenitis, 3% from meningitis, 3% from mastitis, 3% from ascending cholangitis, 3% from prostatitis); *Streptococcus milleri* from abscesses; Group C *Streptococcus* (*Streptococcus equisimilis*, *Streptococcus zooepidemicus, Streptococcus equi*) in cardiovascular disease and malignancy; 21% from respiratory tract, 18% gastrointestinal tract, 17% skin; case-fatality rate 25%), Group D streptococci (3-5% of total cases, 2% of community acquired, 3% of nosocomial, 1% of neonatal, 8% of long term care; case-fatality rate 32% overall, 7% in nosocomial; 87-99% of isolates true infection; 81% hospital acquired; 30% from wound, 22% multiple, 22% abscess, 12-22% genitourinary tract, 8-17% hepatobiliary, 6% gastrointestinal tract, 4% endocarditis, 2% pneumonia; *Enterococcus* common in neutropenics, in immunosuppression with debilitation, following instrumentation, after long term hospitalisation, and subsequent to use of cephalosporins; third most common organism in nosocomial infections in cancer patients; *Enterococcus avium* in gastrointestinal tract abnormalities; *Streptococcus equinus* indicator of possible colonic carcinoma and may cause such complications as endocarditis, spondylodiskitis, vertebral osteomyelitis and splenic abscess), *Streptococcus viridans* (41% *Streptococcus mitis*, 22% *Streptococcus sanguis,* 13% *Streptococcus morbillorum,* 7% *Streptococcus intermedius,* 7% *Streptococcus constellatus*, 2% *Streptococcus salivarius*, 2% *Streptococcus mutans*; 3-5% of all cases, 23% of neonatal; common in neutropenics; case-fatality rate 13%; 52-72% of isolates true infection; 31% clinically significant; 43% from respiratory tract, 29% from abscess, 17% unknown; predisposing factors epistaxis, bone marrow transplantation, treatment with cotrimoxazole, neutropenia), *Bacteroides* (2-6% of total cases, 2% of community acquired, 4% of nosocomial, 11% of neonatal; 11% of cases in solid tumours (case-fatality rate 4%); intermediate frequency in neutropenics; case-fatality rate in nosocomial 35%, overall 9-32%; all isolates true infection; 6-86% of isolates significant; 51% community acquired; 44% from gastrointestinal tract, 35% abscess, 20% wound, 12% hepatobiliary, 4-26% genitourinary tract, 4% bone and joint, 4% pneumonia; *Bacteroides fragilis* 70% of anaerobes isolated, involved in 62% of septicemia associated with infections of the female genital tract; 33% of isolates clinically significant; case-fatality rate 24%; other *Bacteroides* species 6-9% of anaerobes isolated), *Serratia* (2-4% of total cases, 1% of community acquired, 2% of nosocomial, 1% of long term care; uncommon in neutropenics; 93-100% of isolates true infection; 98% clinically significant; 92% nosocomial; 35% multiple, 30-31% respiratory, 8% wound, 8% gastrointestinal tract, 4-30% genitourinary tract, 4% endocarditis, 4% hepatobiliary; case-fatality rate 18-54% overall, 40% in nosocomial), *Brucella* (2% of community acquired; all isolates true infection; septicemia due to *Brucella melitensis* is known as Bruce septicemia or melitensis septicemia), *Tsukamurella pulmonis* and *Tsukamurella tyrosinosolvans* immunosuppressed patients with indwelling venous catheters), *Candida* (1-4% of all cases, 6% of nosocomial, 1% of long term care; fourth most common organism in cancer patients; 5% in leukemia and lymphoma, 9% in solid tumours; case-fatality rate 72% in leukemia and lymphoma, 42% in solid tumours, 29% in nosocomial; *Candida albicans* 51% of fungal isolates, *Candida tropicalis* 13%, *Candida krusei* 9%, *Candida parapsilosis* 6%, *Candida guilliermondii* 6% (1% of catheter associated); *Candida lusitaniae* 1% of catheter associated fungal, *Candida pseudotropicalis* 1%; 57% of *Candida tropicalis* isolates contaminants, all isolates of other species true infection; 93% clinically significant; 96% hospital acquired; 39% from i.v. cannula, 22% unknown source, 20% from gastrointestinal tract; largely in cancer patients receiving parenteral antimicrobials or alimentation; significant risk in patients with urological pathology undergoing surgery or manipulation; also in pregnancy, following abortion or postpartum), *Proteus* (1-3% of total cases, 4% of community acquired, 2% of nosocomial, 13% of long term care; intermediate frequency in neutropenics; 6% of cases in solid tumours (case-fatality rate 42%); overall case-fatality rate 20%, 8% in nosocomial; all isolates true infection; 93% clinically significant; 71% hospital acquired; 25-50%

from genitourinary tract, 25% multiple, 17% abscess, 10% intravascular, 10% wound, 5-17% hepatobiliary, 0-17% respiratory tract), *Enterobacter* (1-3% of total cases, 1% of community acquired, 5-6% of nosocomial, 1% of long term care; intermediate frequency in neutropenics (11%); tenth most common organism in nosocomial infections in cancer patients; 85-100% of isolates true infection; 96% clinically significant; significant underlying conditions, including malignancy, in nearly all cases; 29% from wound, 19% multiple, 12% hepatobiliary tract, 7% intravascular catheter, 7% gastrointestinal tract, 5-33% genitourinary tract, 2-33% respiratory tract, 2% endocarditis; case-fatality rate 18-29% overall, 10% in nosocomial), *Clostridium* (1-2% of total cases, 2% of community acquired; intermediate frequency in neutropenics; 3% of cases in solid tumours (case-fatality rate 67%); overall case-fatality rate 43%; 28% of anaerobes isolated; 99-100% of isolates true infection; vast majority of cases follow septic abortion; also from gastrointestinal tract; *Clostridium perfringens* 6% of anaerobes isolated, 50% of isolates true infection, 10% of isolates clinically significant, 58% hospital acquired, case-fatality rate 43%; *Clostridium septicum* 2% of anaerobic isolates, 3% of isolates clinically significant, case-fatality rate 40%; *Clostridium oedematiens*, *Clostridium difficile* in immunocompromised; *Clostridium tertium* in neutropenics and aspiration pneumonia, 13% of anaerobes isolated), *Peptostreptococcus* (1% of total cases; common in neutropenics; 3% of anaerobes isolated; all isolates true infection; 3% of isolates clinically significant; 25% from surgical wound, 25% from urinary catheter, 25% from i.v. catheter, 25% biliary; case-fatality rate 9%), *Neisseria meningitidis* (meningococcal bacteraemia (meningococcaemia; 43% of meningococcal infections;) is a mild systemic disease which, on rare occasions, may become chronic; meningococcal septicemia (meningococcal fever; 5-20% of meningococcal infections) is a severe disease with large numbers of meningococci in bloodstream, usually accompanied by severe toxemia due to meningococcal endotoxins, but without disseminated intravascular coagulation and, as a rule, without meningitis, and which may be acute or chronic; incidence 0.2/100,000; 1% of community acquired; all isolates true infection; case-fatality rate 25%), *Haemophilus influenzae* (nontypeable strains; 0.7-4% of total cases, 1% of community acquired, 1% of nosocomial, 1% of neonatal, 0.5% of long term care; intermediate frequency in neutropenics; 94-100% of isolates true infection; 94% clinically significant; 60% community acquired; 100% from respiratory tract; clinical presentation in older children and adults: 52% pneumonia, 27% septicemia, 8% meningitis, 5% gynecologic infection, 5% epiglottitis; 31-36% mortality), diphtheroids (3% of isolates; 71% of isolates contaminants; 16% clinically significant), *Bacillus* (1% of total isolates; 91-94% of isolates contaminants; 4% clinically significant; in compromised; uncommon in neutropenics; usually *Bacillus cereus; Bacillus anthracis* marked toxic effects), *Neisseria* species other than *Neisseria meningitidis* and *Neisseria gonorrhoeae* (0.5% of isolates; 33% contaminants; 50% clinically significant; *Neisseria cinerea, Neisseria flavescens, Neisseria lactamica, Neisseria subflava*; uncommon in neutropenics and other immunodeficient), *Peptococcus* (0.4% of isolates; 88% of isolates true infection; 78% clinically significant; mainly obstetrical patients during peripartum period; also 1% of neonatal cases; uncommon in neutropenics), *Fusobacterium* (0.3% of isolates, 9% of anaerobic isolates; 50% clinically significant, 50% transient bacteremia; intermediate frequency in neutropenics; *Fusobacterium necrophorum* all isolates true infection; 33% from genitourinary tract, 33% respiratory, 33% abscess; 1% of neonatal cases; intermediate frequency in neutropenics), *Citrobacter* (0.3% of isolates; all isolates clinically significant; uncommon in neutropenics; 0.5% of long term care; case-fatality rate 17%), *Listeria monocytogenes* (0.2% of isolates; all isolates true infection; 75% clinically significant; 57% community acquired; 60% from CNS; 4% of neonatal cases; uncommon in neutropenics), *Campylobacter* (0.1% of all isolates; all isolates clinically significant; *Campylobacter fetus* subsp *fetus*, *Campylobacter jejuni* (in conjunction with gastroenteritis in people at extremes of age or with cirrhosis, diabetes, renal failure, cancer, HIV), *Campylobacter coli, Campylobacter upsaliensis, Campylobacter lari, Arcobacter butzleri*), *Capnocytophaga* (0.1% of isolates; all clinically significant; especially with oral mucositis; uncommon in neutropenics; *Capnocytophaga canimorsus* in hemochromatosis, asplenia or alcoholism following dog or cat bite), *Moraxella* (0.1% of isolates; 33% contaminants, 67% transient bacteraemia; uncommon in neutropenics; *Moraxella catarrhalis* rare in immunodeficient; *Moraxella osloensis*), *Providencia* (0.1% of isolates; all isolates clinically significant; uncommon in neutropenics; case-fatality rate 9%; *Providencia stuartii* 13% of long term care; *Providencia rettgeri* 0.5% of long term care), *Eubacterium lentum* (0.08% of isolates; 50% contaminants, 50% clinically significant), *Haemophilus aegytius* (Brazilian purpuric fever), *Haemophilus aphrophilus, Chromobacterium violaceum* (acute septicemia associated with abscesses in multiple organs; uncommon in neutropenics), *Yersinia pestis*, *Yersinia enterocolitica* (in iron overload cirrhosis; uncommon in neutropenics), *Mycoplasma hominis* (6% of neonatal cases), *Ureaplasma urealyticum* (1% of neonatal cases, puerperal), *Mycobacterium fortuitum* and *Mycobacterium chelonae* (catheter related), *Vibrio vulnificus* (elevated iron due to hemochromatosis or alcoholism), *Vibrio metschnikovii*, *Vibrio cholerae* non-01 (in cirrhosis and leukemia), *Vibrio cincinnatii, Vibrio hollisae* and *Vibrio parahaemolyticus* (following ingestion of seafood), *Flavobacterium meningosepticum* (in leukemia; uncommon in neutropenics), *Aeromonas* (uncommon in neutropenics; *Aeromonas hydrophila* $\approx$ 50% case-fatality rate in immunocompromised), *Alcaligenes* (uncommon in neutropenics; *Alcaligenes xylosoxidans xylosoxidans* rare catheter related and gastrointestinal, especially in cancer patients), *Francisella tularensis*, *Kingella kingae* (mainly children; uncommon in neutropenics), *Anaerobiospirillum succiniciproducens*, *Corynebacterium* (27% of isolates contaminants; *Corynebacterium jeikeium* 90% catheter related; *Corynebacterium urealyticum* in immunosuppressed; *Corynebacterium striatum* in imunocompromised or anatomically altered patients), *Staphylococcus saprophyticus* (rare cases associated with sexual intercourse and/or urinary obstruction), *Leuconostoc* (rare cases associated with parenteral nutrition, other catheters and previous antibiotic therapy), *Oerskovia*

(catheter related), *Propionibacterium acnes* (associated with foreign body; intermediate frequency in neutropenics; 33% of anaerobic isolates; 3% of isolates clinically significant; case-fatality rate 45%), *Gardnerella vaginalis* (obstetric patients, rarely from prostate in males; uncommon in neutropenics), *Zymomonas* (uncommon in neutropenics), *Legionella* (uncommon in neutropenics), *Eikenella corrodens* (uncommon in neutropenics), *Acinetobacter* (uncommon in neutropenics; *Acinetobacter baumannii* nosocomial; *Acinetobacter johnsonii* vascular catheter related), *Shigella* (uncommon in neutropenics), *Erwinia* (uncommon in neutropenics), *Hafnia* (uncommon in neutropenics), *Edwardsiella tarda* (exposure to aquatic environments or exotic animals, preexisting liver disease, iron overload, raw fish ingestion; uncommon in neutropenics), *Morganella* (uncommon in neutropenics; 3% of long term care), *Actinobacillus* (uncommon in neutropenics; *Actinobacillus actinomycetemcomitans* also associated with oral infection), *Veillonella* (uncommon in immunocompromised), *Pediococcus acidilacti* (severely compromised), *Neisseria gonorrhoeae*, *Erysipelothrix rhusiopathiae*, *Actinomyces israelii* (usually from pulmonary actinomycosis), *Stenotrophomonas maltophilia* (0.5% of long term care; nosocomial infection in immunocompromised patients receiving broad spectrum antimicrobials), *Leptotrichia buccalis* (in cancer patients), *Pseudomonas luteola* and *Pseudomonas oryzihabitans* (prosthetic materials, corticosteroids), *Rothia mucilaginosa* (i.v. drug abuse, cardiac valve disease, vascular catheters, immunocompromised), *Ochrobacterium anthropi* (catheter associated), *Methylobacterium extorquens* (catheter related), *Agrobacterium tumefaciens* (intravascular catheter), *Prevotella melaninogenica* (8% of septicemia associated with female genital tract infection), *Sphingobacterium multivorum* (haemodialysis, lymphoma), *Weeksella virosa* (postsurgical), *Plesiomonas shigelloides* (secondary to cellulitis and prostatitis), *Pasteurella multocida* (following pneumonia), *Helicobacter cinaedi* and *Helicobacter fennelliae* (in homosexual men), *Cardiobacterium hominis, Succinivibrio dextrinosolvens* (rare cases associated with gastrointestinal or oesophageal sepsis), *Ochrobactrum anthropi* (patients on haemodialysis), *Brevibacterium casei* (associated with Hickmann catheter in AIDS), *Bartonella quintana* (homeless), *Bartonella bacilliformis* (Oroya fever), *Candida glabrata* (solid tumours and nononcologic; 13% of fungal isolates; 4% of catheter associated), *Malassezia furfur* and *Malassezia pachydermatis* (patients receiving i.v. fat emulsions; 1% of catheter associated fungemia in cancer patients), *Saccharomyces cerevisiae* (1% of catheter associated fungemia in cancer patients), *Trichosporon*, *Fusarium, Rhodotorula rubra* and *Pichia* in cancer patients; 6-14% of cases polymicrobial (82% hospital acquired; 74% severe underlying illness; case-fatality rate 21->50%)

Diagnosis: blood cultures; counterimmunoelectrophoresis of serum; white cell count 4,300-11,400 (mean 8160/μL), neutrophils 24-83% (mean 61%), shift to left with 5-56% (mean 25%) bands, toxic granulation, lymphocytes 5-17% (mean 10%), monocytes 0-6% (mean 3%), eosinophils 0-35% (mean 1%), basophils 0-1% (mean 1%); fibrin degradation products normal or elevated (significant elevation in 70% of cases), daily estimations may indicate patient's progress; platelet aggregation normal in 30-50% of cases; platelet count 90,000-468,000/μL; infarction, Addisonian crisis (extremely rare) may simulate

Gram Negative: increasing age, underlying medical condition, surgery or trauma, invasive diagnostic procedures, mechanical ventilatory support, antimicrobial treatment, immunosuppressive agents, vascular or bladder indwelling catheters; fever in 90-95%, change in mental status in 60-70%, increased respiratory rate in 50-60%, chills in 50%, hypotension in 40-60%, oliguria in 30-50%, bleeding from needle-sticks or mucosal surfaces in 7-10%, hypothermia in 5-10%, skin lesions in 5-10%; positive blood cultures in 100%, leucocytosis in 85-90%, acidosis in 50-80%, elevated blood urea nitrogen and/or creatinine in 50-80%, thrombocytopenia in 50-60%, abnormal liver function tests in 20-30%, leucopenia in 10-15%

Brazilian Purpuric Fever: child 3 mo - 1 y, acute febrile illness, abdominal pain or vomiting, hemorrhagic skin lesions, history of conjunctivitis in 30 d preceding fever, no evidence of meningitis

Gonococcal Septicemia: often fever and rigours

Meningococcal Septicemia: retinal haemorrhages common

Septicemia Due to *Clostridium*: high fever, extensive intravascular haemolysis, acute renal tubular necrosis; usually fatal

Listerial (Listeric) Septicemia: usually predominant involvement of liver

***Erysipelothrix rhusiopathiae* Septicemia:** fever, generalised myalgia, anorexia, weight loss; often results in endocarditis

Neonatal: absence of specific antibodies, polymorphonuclear dysfunction, decreased complement, prematurity, prolonged rupture of membranes, complicated delivery, maternal infection, ventilatory support equipment, intravascular monitoring devices, bladder catheters; temperature may be normal or low (elevated in only 40%), evidence of respiratory distress including apnoea, poor feeding, jaundice; leucopenia with increased percentage of band forms; positive cultures

Anthrax: Gram stain, India ink stain and culture of blood; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test

Bacillus cereus: diarrhoea, fever, altered mental status; Gram stain and culture of blood

***Brucella*:** acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Treatment: volume repletion (including colloids), rapidly infused; oxygen under pressure if necessary; vasopressor amines in elderly patients with coronary insufficiency and normal central venous pressure; ? polymxyin B in Gram negative; monitor blood glucose

Infection From Female Genital Tract: amoxy(ampi)cillin 2 g i.v. 6 hourly + gentamicin 4-6 mg/kg i.v. as single daily dose + metronidazole 500 mg i.v. 12 hourly or 1 g rectally 8 hourly

Penicillin Hypersensitive (Not Immediate), Sexually Acquired: doxycycline 100 mg orally or i.v. 12 hourly + cefoxitin 2 g i.v. 8 hourly, doxycycline 100 mg orally or i.v. 12 hourly + metronidazole 500 mg i.v. 12 hourly + ceftriaxone 1 g i.v. daily or cefotaxime 1 g i.v. 8 hourly

Immediate Penicillin Hypersensitivity, Postpartum: gentamicin 4-6 mg/kg as single daily dose (adjust dose for renal function) + clindamycin 600 mg i.v. slowly 8 hourly or lincomycin 600 mg i.v. 8 hourly

Elderly, Diminished Renal Function: cefotaxime 1 g i.v. 8 hourly or ceftriaxone 1 g once daily + metronidazole as above; piperacillin-tazobactam 4/0.5 g i.v. 8 hourly or ticarcillin-clavulanate 3/0.1 g i.v. 6 hourly

Infection from Respiratory System:

Adults: erythromycin 0.5-1 g i.v. slowly 6 hourly + cefotaxime 1 g i.v. 8 hourly or ceftriaxone 1 g i.v. once daily or benzylpenicillin 1.2 g i.v. 4-6 hourly + gentamicin 5-7 mg/kg i.v. daily

Children: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly + cefotaxime 50 mg/kg to 2 g i.v. 6-8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. once daily or chloramphenicol 75 mg/kg/d to 3 g/d i.v. in 3 divided doses

Focus Probably Biliary or Gastrointestinal Tract (Including Ascending Cholangitis): gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. as single daily dose (adjust dose for renal function) + metronidazole 12.5 mg/kg to 500 mg i.v. infused over 20 min 12 hourly or 1 g (< 12 y: 500 mg) rectally 8-12 hourly + amoxy(ampi)cillin 50 mg/kg to 2 g i.v. 6 hourly; clindamycin 600 mg i.v. 8 hourly (child > 1 mo: 15-40 mg/kg daily in divided doses) + gentamicin as above; when afebrile, change to amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally for total of 7 d

Elderly Patients With Diminished Renal Function, Significantly Elevated Serum Creatinine or Other Contraindication to Gentamicin: piperacillin-tazobactam 100/12.5 mg/kg to 4/0.5 g i.v. 8 hourly or ticarcillin-clavulanate 50/1.7 mg/kg to 3/0.1 g i.v. 6 hourly

Penicillin Hypersensitive (Not Immediate): metronidazole 12.5 mg/kg to 500 mg i.v. 12 hourly + ceftriaxone 25 mg/kg to 1 g i.v. once daily or cefotaxime 25 mg/kg to 1 g i.v. 8 hourly

Immediate Penicillin Hypersensitivity: substitute vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly) for amoxy/ampicillin

Focus Probably Urinary Tract: amoxy(ampi)cillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. as single daily dose (adjust dose for renal function)

Penicillin Hypersensitive: gentamicin alone

Aminoglycoside Contraindicated: ceftriaxone 50 mg/kg to 1 g i.v. once daily, cefotaxime 50 mg/kg to 1 g i.v. 8 hourly

Focus Probably Open Skin Infection/Cellulitis: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly; if penicillin hypersensitive, cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 50 mg/kg to 2 g i.v. 8 hourly if not immediate, or clindamycin 10 mg/kg to 450 mg i.v. or orally 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly or vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

Children < 4 y with Facial or Periorbital Cellulitis: as above + cefotaxime 50 mg/kg to 2 g i.v. 8 hourly or ceftriaxone 50 mg/kg to 2 g once daily or chloramphenicol 75 mg/kg/d to maximum 3 g/d i.v. in 3 divided doses

Focus Probably Decubitus or Ischaemic Ulcer or Diabetic Foot Infection: surgical debridement of necrotic tissue; piperacillin + tazobactam 4 + 0.5 g i.v. 8 hourly, ticarcillin-clavulanate 3/0.1 g i.v. 6 hourly, meropenem 500 mg i.v. 8 hourly; if penicillin hypersensitive, ciprofloxacin 400 mg i.v. or 750 mg orally 12 hourly + clindamycin 900 mg i.v. 8 hourly by slow infusion or lincomycin 900 mg i.v. 8 hourly by slow infusion

Focus Probably Intravascular Device (Including Central Venous Lines): remove and culture cannula; di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly for 2 w + gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) as single daily dose (adjust dose for renal function)

Penicillin Hypersensitive (Not Immediate): substitute cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 50 mg/kg to 2 g i.v. 8 hourly for di/flucloxacillin

Immediate Penicillin Hypersensitivity or MRSA a Possibility: substitute vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. slowly 12 hourly (monitor blood levels and adjust dose accordingly) for di/flucloxacillin

Elderly, Diminished Renal Function: flucloxacillin + cefotaxime 1-2 g i.v. 8 hourly or ceftriaxone 1-2 g i.v. once daily

Unidentified Source:

Normal Adult: gentamicin 4-6 mg/kg i.v as single daily dose (adjust dose for renal function) + di(flu)cloxacillin 2 g i.v. 4-6 hourly or (if non-immediate penicillin hypersensitivity) cephalothin 2 g i.v. 6 hourly or cephazolin 2 g i.v. 8 hourly or (immediate penicillin hypersensitivity) vancomycin 25 mg/kg to 1 g i.v. by slow infusion 12 hourly (monitor blood levels and adjust dose accordingly)

Child:

Meningitis Not Excluded:

< 6 mo: amoxy/ampicillin 50 mg/kg i.v. 6 hourly + cefotaxime 50 mg/kg i.v. 6 hourly + (if pneumococcal meningitis likely) vancomycin 15 mg/kg i.v. 6 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

> 6 mo: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly + cefotaxime 50 mg/kg to 2 g i.v. 6 hourly or ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly + (if pneumococcal meningitis is likely) vancomycin 15 mg/kg to 500 mg i.v. 6 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

Meningitis Excluded:

< 4 mo: amoxy/ampicillin 50 mg/kg i.v. 6 hourly + gentamicin 7.5 mg/kg i.v. daily (adjust dose for renal function)

> 4 mo: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly + cefotaxime 25 mg/kg to 1 g i.v. 6 hourly or ceftriaxone 25 mg/kg to 1 g i.v. daily

Febrile Neutropenic Patients: ceftazidime 50 mg/kg to 2 g i.v. 8 hourly, piperacillin + tazobactam 100 + 12.5 mg/kg to 4 + 0.5 g i.v. 8 hourly, gentamicin 4-6 mg/kg (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function) + ticarcillin-clavulanate 50/1.7 mg/kg to 3/0.1 g i.v. 6 hourly; + (if Gram positive organism resistant to other agents isolated or clinical progression) vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1 g i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

In every case, institute appropriate specific therapy as soon as laboratory results are available:

***Salmonella*:** amoxycillin 1 g i.v. 6 hourly (< 20 kg: 25-50 mg/kg daily in divided doses), chloramphenicol 500 mg orally 6 hourly (child > 2 w: 50 mg/kg/d orally in 4 divided doses; premature, newborn and those with immature metabolism: 25 mg/kg/d in 4 divided doses), cotrimoxazole 160/800 mg i.v. or orally (6 w - 5 mo: 20/100 mg i.v.; 6 mo - 5 y: 40/200 mg i.v.; 6-12 y: 80/400 mg) 12 hourly (severe infection in child: 6/30 mg/kg i.v. daily in 2 divided doses), ofloxacin

Shigella: ampicillin 200 mg/kg i.v. in divided doses daily ± gentamicin 1.3 mg/kg i.v. 8 hourly

Other Gram Negative Enteric Bacteria: gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. daily (adjust dose for renal function), ceftriaxone 50 mg/kg to 1 g i.v. daily, cefotaxime 50 mg/kg to 1 g i.v. 8 hourly

Staphylococci: careful investigation to determine if associated endovascular or metastatic focus

Penicillin Susceptible *Staphylococcus aureus:* benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly

Penicillin Resistant Methicillin Susceptible *Staphylococcus aureus*: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly, cephazolin 50 mg/kg to 2 g i.v. 8 hourly

Methicillin Resistant *Staphylococcus aureus*, Coagulase Negative Staphylococci, Immediate Penicillin Hypersensitivity: vancomycin 25 mg/ kg (< 12 y: 30 mg/kg) to 1 g i.v. 12 hourly over 60 min (monitor blood levels and adjust dose accordingly)

Streptococcus pneumonia: broad spectrum cephalosporin + vancomycin until sensitivities available

Burkholderia pseudomallei: cotrimoxazole + ceftazidime or meropenem or imipenem

Anaerobiospirillum succiniciproducens: cephamandole 1 g every 8 h

***Neisseria meningitidis*:** i.v. fluids, oxygen and ventilation support, inotropic agents if fluid resuscitation unsuccessful, dexamethasone 0.6 mg/kg/d in 4 divided doses if cerebral edema and increased intracranial pressure; activated protein C; benzylpenicillin (< 1 y: 300 mg; 1-9 y: 600 mg; ≥ 10 y: 1200 mg) i.v. or i.m. before hospital transfer, then 45 mg/kg to 1.8 g i.v. 4 hourly for 3-5 d

Penicillin Hypersensitive (Not Immediate) or Remote Areas: ceftriaxone 50 mg/kg to 2 g i.v. immediately, then ceftriaxone 100 mg/kg to 4 g i.v. daily, 50 mg/kg to 2 g i.v. 12 hourly for 3-5 d or cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 3-5 d

Capnocytophaga canimorsus, Leptotrichia buccalis: penicillin

***Pseudomonas aeruginosa*:** ticarcillin-clavulanate 50/1.7 mg/kg to 3/0.1 g 4 hourly + gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. as single daily dose

Penicillin Hypersensitive (Not Immediate Hypersensitivity): ceftazidime 50 mg/kg to 2 g i.v. 8 hourly by infusion over 30 minutes or cefepime 50 mg/kg to 2 g i.v. 12 hourly or cefpirome 50 mg/kg to 2 g i.v. 12 hourly + gentamicin as above

Immediate Penicillin Hypersensitivity: ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly + gentamicin as above

Burkholderia cepacia: imipenem

***Alcaligenes xylosoxidans*:** cotrimoxazole, ciprofloxacin

***Leuconostoc*:** high dose penicillin, clindamycin; removal of intravascular catheters when appropriate

***Oerskovia*:** ampicillin + cotrimoxazole

Bacillus, Rothia mucilaginosa, Corynebacterium jeikeium, Corynebacterium striatum, Corynebacterium urealyticum: vancomycin 500 mg i.v. over 60 minutes 6 hourly (child: 44 mg/kg i.v. daily in divided doses over 60 minutes) + carbapenem

Yersinia enterocolitica*, *Campylobacter fetus* subsp *fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens: gentamicin 1.3 mg/kg (child 1.5-2.5 mg/kg) i.v. 8 hourly ± amoxycillin-clavulanate, piperacillin, cotrimoxazole, rifampicin, fluoroquinolone

Other *Campylobacter*: ciprofloxacin

***Stenotrophomonas maltophilia*, *Ochrobacterium antropi*:** cotrimoxazole

***Acinetobacter*:** colistimethate sodium 2.5 mg/kg to 300 mg i.v. 12 hourly

***Enterococcus*:** ampicillin + gentamicin (streptomycin if high level resistance to gentamicin and streptomycin susceptible); vancomycin

Vibrio: doxycycline 100 mg orally or i.v. twice daily + ceftazidime 2 g i.v. 3 times a day or ciprofloxacin 400 mg twice a day for 3 d or gentamicin

Candida albicans: fluconazole 10 mg/kg to 400 mg i.v. once daily till clinical improvement, then 10 mg/kg to 400 mg orally daily to complete total of at least 2 w

Other Fungi: catheter removal + amphotericin B desoxycholate 0.5-1 mg/kg in glucose 5% i.v. infusion (preferably through a central line) slowly over 2-6 h (following test dose) once daily till clinical improvement then fluconazole 10 mg/kg to 400 mg orally daily for at least 14 d or (*Candida krusei, Candida glabrata*) voriconazole or caspofungin

Prophylaxis:

Post-Splenectomy: asplenic children and children with sickle cell anemia < 5 y, first 2 y following splenectomy, patients with severe underlying immunosuppression

< 24 mo Old: amoxycillin 20 mg/kg orally once daily, phenoxymethylpenicillin 125 mg orally twice daily

> 2 y Old: amoxycillin 250 mg orally once daily, phenoxymethylpenicillin 250 mg orally 12 hourly

Penicillin Hypersensitive: roxithromycin 4 mg/kg to 150 mg orally once daily, erythromycin 250 mg orally once daily, erythromycin ethyl succinate 400 mg orally daily

Neisseria meningitidis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

Cirrhotic Patient with Gastrointestinal Bleeding: norlfloxacin 400 mg orally commencing 1 h before endoscopy and then 12 hourly for 1-2 d or if oral therapy not feasible ciprofloxacin 400 mg i.v. at time of induction and then 12 hourly for 1-2 d

Streptococcus pneumonia: pneumococcal polysaccharide vaccine recommended to adults ≥ 65 y, individuals > 2 y with chronic illness, anatomic or functional asplenia, immunocompromise (disease, chemotherapy, steroids), HIV infection, environment or settings with increased risk, or cochlear implants; pain, swelling and redness at injection site in 30-50%, fever and muscle aches in < 1%, rare severe reactions; revaccination after 5 y for ≥ 2 y with functional or anatomic asplenia, immunsuppression, malignancy, transplant, chronic renal failure, nephritic syndrome, HIV infection, chronic systemic steroids, or < 65 y at time of first vaccination; pneumococcal conjugate vaccine recommended for routine vaccination of children < 24 mo and 24-59 mo with high risk medical conditions; pain, swelling and redness at injection site in 10-20%; reduces invasive disease due to serotypes in the vaccine by 97% and to those not in the vaccine by 89%

Septicemic Adrenal Hemorrhage Syndrome (Adrenal Hemorrhage Syndrome, Sepsis Acutissima Hyperergica Fulminans, Septicemic Adrenal Hemorrhage): fulminating, usually fatal, form of septicemia; mechanism not clearly understood

Agent: usually *Neisseria meningitidis* (fulminating purpuric meningococcemia, Marchand-Waterhouse-Freiderichsen syndrome, meningococcal hemorrhagic adrenalitis, meningococcal adrenal syndrome, Waterhouse-Friderichsen syndrome); also

Streptococcus pneumoniae, *Streptococcus pyogenes*, *Staphylococcus*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, several members of Enterobacteriaceae

Diagnosis: sudden onset of fever, chills, myalgia, vomiting, headache, cyanosis/hemorrhage of skin and mucous membranes, bilateral adrenal hemorrhage, disseminated intravascular coagulation and shock; blood cultures

Treatment: supportive; antimicrobials depending on agent

Subacute Febrile Disease

Agents: streptococci (mainly *Streptococcus viridans*), any bacterium

Diagnosis: blood cultures

Treatment: dependent on isolate

Chronic and Sub-acute Fever

Agents: *Candida albicans*, *Candida lusitaniae* (in immunocompromised), *Cryptococcus neoformans*, *Histoplasma capsulatum*

Diagnosis: blood cultures (DuPont Isolator, Bactec); moderate anemia (normochromic normocytic becoming hypochromic); raised ESR

Treatment: amphotericin B 0.75 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2 w; fluconazole 800 mg/kg orally or i.v. initially, then 400 mg daily

Sweating Disease (Miliary Fever, Sweating Sickness): acute febrile infectious disease; no reference in literature during past 25 years

Agent: ? *Chlamydia*

Diagnosis: profuse sweating and formation of numerous papules

Treatment: presumably, doxycycline or erythromycin

Pseudobacteremia: 11% of nosocomial epidemics; 55% contaminated during specimen collection, handling and processing (non-sterile blood collection tubes, cross contamination by obtaining blood culture and other specimens from same venipuncture, contaminated skin preparation material, contaminated blood culture tube holders, contaminated commercial culture media, contaminated commercial radiometric analyser, contaminated tincture of thiomersal used to sterilise blood culture bottle tops, inadequately sterilised integral stoppers, other contaminated equipment, disinfectants and vascular catheters)

Agents: variety of organisms, including *Aerococcus viridans*, *Burkholderia cepacia, Stenotrophomonas maltophilia*

Transfusion Reactions Due to bacterial Contamination of Blood and Blood Products: mortality 35%

Agents: wide range of bacteria, most commonly *Pseudomonas fluorescens* and other *Pseudomonas* species

Diagnosis: 80% fever, 53% chills, 37% hypotension, 26% nausea/vomiting; smear and culture of transfused product at 4°C, 25°C and 35°C; culture of patient's blood

Treatment: antimicrobials as suggested by smear

Endotoxinemia

Agents: *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterobacter agglomerans*

Diagnosis: fever, chills; limulus test, SimpliRED endotoxin agglutination test

Treatment: supportive; removal of contaminated equipment (eg, hemodialysis); polymxyin B

Toxic Shock Syndrome (Tampon Disease, TSS): a characteristic generalised toxemia associated with toxin production at a carrier site (including, notably, the vagina) or in a local lesion; case-fatality rate 3%

Agent: toxin-producing strains of *Staphylococcus aureus*; associated with tampons, barrier contraceptives, postpartum, surgical wound infections, focal staphylococcal infections, nasal surgery, sinusitis, influenza in children; also due to *Streptococcus pyogenes* (mainly associated with cellulitis, varicella and use of non-steroidal antiinflammatory drugs); cases due to *Campylobacter intestinalis, Streptococcus agalactiae* and *Streptococcus canis* reported

Diagnosis:

Staphylococcal: fever > 38.9°C in all cases; generalised scarlatiniform (diffuse macular erythematous) skin rash in all cases; mild skin desquamation (particularly of palms and soles) in convalescence (1-2 w after onset of illness) in all cases; hypotension, tachycardia, myocarditis, pericarditis, tachyarrhythmia in 91-95%; diarrhoea or vomiting at onset of illness, ileus, melena, hepatomegaly, hepatic necrosis, acute pancreatitis, acute abdomen in 42-62%; disorientation, meningismus, coma, seizure, cerebral edema in 24-50%; profound myalgia or arthralgia lasting > 5 d in 25-52%; tachypnoea, pleural effusion, pleural edema, acute respiratory distress syndrome in 24-33%; pharyngitis or conjunctivitis lasting > 5 d, strawberry tongue in 21-29%; oliguria, azotemia, acute tubular necrosis, acute renal failure in 0-17%; vaginal, oropharyngeal, conjunctival hyperemia, vulvar edema; late sequelae: nail or hair loss, delayed venous capillary filling in 45-56%, impaired memory or concentration, ataxia, dysarthria in 38-67%, neuromyasthenia, chronic fatigue in 33-54%, menstrual irregularity, menorrhagia, dysmenorrhoea in 25-31%, cardiomyopathy, congestive heart failure, recurrent syncope in 0-23%, chronic diarrhoea, weight loss, anorexia; electrocardiogram (decreased voltage and ST-T wave changes in 20% of cases, new gallop rhythms in 5%); elevated blood urea nitrogen (≥ 2X upper limit normal in 52% of cases), serum creatinine (≥ 2X ULN in 52%), bilirubin (≥ 1.5X ULN in 54%), creatine phosphokinase (≥ 2X ULN in 59%), SGOT (≥ 2X ULN in 42%), SGPT (≥ 2X

ULN in 42%); white cell count with marked left shift, platelet count low in first week (≤ 100,000/μL in 42%), usually high in second week (≥ 400,000/μL in 27%); urinalysis (≥ 5 leucocytes/hpf, ≥ 1 erythrocyte/hpf and protein ≥ 1+ in 88%); isolation of *Staphylococcus aureus* from cervical or vaginal swabs confirmatory but never diagnostic; tests for toxin production not suitable for routine laboratory use; negative tests for blood (bacteremia in < 3%), throat, CSF cultures and serological tests for Rocky Mountain spotted fever, leptospirosis and measles

Streptococcal: severe pain, fever, shock, hypotension, renal impairment, coagulapathy, liver involvement, adult respiratory disease, generalised erythematous rash (less likely), soft tissue necrosis; blood cultures positive in 60%

Differential Diagnosis: mild forms of toxic epidermal necrolysis (absence of Nikolsky's sign in TSS), Kawasaki syndrome, staphylococcal scarlet fever (skin biopsy, serologic evidence of exfoliatin), streptococcal scarlet fever (ASOT), Rocky Mountain spotted fever (petechial rash), leptospirosis, meningococcemia (petechial or purpuric rash), Stevens-Johnson syndrome

Treatment:

Staphylococcus aureus: remove tampon; administer fluid replacement therapy; search for possible sites of infection (culture from vagina, oropharynx, conjunctiva, wounds, blood and urine)

Methicillin Sensitive: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly, cephazolin 50 mg/kg to 2 g i.v. 8 hourly

Methicillin Resistant, Immediate Penicillin Hypersensitivity: vancomycin 500 mg i.v. 6 hourly over 60 minutes (child: 44 mg/kg i.v. daily in divided doses)

Streptococci: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly + clindamycin 15 mg/kg to 600 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly; normal immunoglobulin 0.4-2 g/kg i.v. for 1 or 2 doses in first 72 h

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly, cephazolin 50 mg/kg to 2 g i.v. 8 hourly

Campylobacter intestinalis: erythromycin

TETANUS (LOCKJAW): 2 notified cases in Australia in 1999; incidence 0.04/100,000 in USA; case-fatality rate 0.5 or higher in general tetanus and 0.01 in local form; neonatal tetanus (tetanus neonatorum, tetanus of the newborn), contracted through contamination of umbilical cord or stump, kills at least 800,000 worldwide each year; transmission by contamination of wound (most frequently, puncture wound; on rare occasions, surgical wound, usually due to faulty sterilisation; 10-20% of cases no wound implicated; 5-10% minor wound or only chronic skin lesions); incubation period few days to several weeks

Agent: *Clostridium tetani* (exotoxin)

Diagnosis: general: spasms of voluntary muscles and episodes of respiratory arrest; local: spasms and muscular rigidity near site of wound (may progress to general); neonatal: usually towards end of first week of life, dysphagia, spasms of facial and neck muscles leading to generalised convulsions and rigidity and death from spasms of respiratory muscles; Gram stain and culture of pus or tissue scrapings; although presence of *Clostridium tetani* is not significant in a fully immunised individual, other *Clostridium* species of very similar morphology may be found in wounds, and diagnosis of tetanus will probably be obvious clinically before it is made in the laboratory, the presence of Gram positive bacilli with typical drumstick morphology of *Clostridium tetani* in primary Gram stain or on culture should be reported immediately to the attending clinician

Treatment: 500-1000 U human tetanus immunoglobulin i.m. or 10 000 U anti-tetanus serum i.v. (? intrathecal tetanus immunoglobulin) + benzylpenicillin 10 MU (child: 50 000-250 000 U/kg) daily i.v. in 4 divided doses for 4 d or cephalosporin or erythromycin (? + prednisolone 40 mg/d orally for 10 d); pyridoxine 100 mg/d; wound debridement

Prophylaxis: highly effective vaccine (3 s.c. injections tetanus-diphtheria toxoid in infancy, with booster doses every 10 y); toxoid in wounded patients + tetanus immunoglobulin if immunisation history uncertain or 0-1 doses (also 2 doses if wound > 24 h old)

WOUND MYIASIS (TRAUMATIC MYIASIS): infestation of wounds by larvae of certain flies

Agents: *Chrysomya megacephala, Cochliomyia hominivorax, Lucilia sericata, Musca domestica, Lucilia cuprina, Lucilia sericata, Phormia regina, Sarcophaga albiceps, Sarcophaga bullata, Sarcophaga carnaria, Peckia chrysostoma, Sarcophaga crassipalpis, Gasterophilus haemorrhoidalis, Sarcophaga misera, Sarcophaga peregrina, Blaesoxipha plinthopyga, Sarcophaga ruficornis, Sarcophaga tibialis, Wohlfahrtia vigil*

Diagnosis: direct visualisation of larvae

Treatment: removal of larvae

Chapter 9

Infections of the Cardiovascular System

Aplastic Crisis

Agent: *human parvovirus B19* in persons with underlying hemolytic disorders

Diagnosis: dot hybridisation, capture ELISA on serum (Biotrin and Dako 100% sensitivity and specificity), PCR

Treatment: supportive

Chronic Anemia

Agent: *human parvovirus B19* in immuncompromised (especially HIV/AIDS)

Diagnosis and Treatment: as above

Babesiosis (Piroplasmosis): America, Ireland, Scotland; transmitted by *Ixodes* tick (black-legged tick, sheep tick) that feeds on deer as an adult but on mice and man in immature stages

Agent: *Babesia bovis* and *Babesia divergens* in splenectomised persons (usually fatal), *Babesia microti* in persons with intact spleen (usually self-limited)

Diagnosis: organisms seen in erythrocytes in Giemsa stained blood films; serology by indirect fluorescent antibody titre; inoculation of patient's blood into splenectomised hamsters or guinea pigs, followed by microscopy of animal's blood

***Babesia bovis* and *Babesia divergens*:** rapid onset, fever, chills, jaundice, dark urine with hemoglobinuria, hypotension, severe anorexia, renal insufficiency

***Babesia microti*:** gradual onset, fever, chills, diaphoresis, myalgia, anemia, fatigue, headache, pulmonary complication (cough, acute respiratory distress; pulmonary edema on chest X-ray)

Treatment: usually not necessary for patients with intact spleen; chloroquine phosphate 1.5 g orally initially followed by 500 mg orally daily for 2 w or clindamycin 1.2 g i.v. 12 hourly (child: 20-40 mg/kg daily in 3 divided doses) or 600 mg orally 8 hourly for 7-10 d + quinine 600 mg orally 8 hourly (child: 25 mg/kg daily in 3 divided doses) for 7-10 d or pentamidine isethionate produce symptomatic improvement but do not reduce parasitemia; exchange transfusion reliably affects rapid reduction of parasite load

(There have been a few reports of intaerythrocytic parasitoses with *Nuttalia* and *Entopolypoides*.)

Malaria (Ague, Cameroon Fever, Chagues Fever, Chills and Fever, Coastal Fever, Congestive Remittent Fever, Corsican Fever, Intermittent Bilious Fever, Intermittent Fever, Jungle Fever, Marsh Fever, Miasmatic Fever, Paludism, Remittent Congestive Fever, Remittent Gastric Fever, Tropical Fever): Africa, Southeast Asia, India, South America; 300-500 M clinical cases/y worldwide (2 M deaths/y); ≈ 700 notified cases/y in Australia (≈ 42% in Queensland); incidence 0.9/100,000 in USA; case-fatality rate 4%; claimed to be responsible for 50% of all human deaths from disease since Stone Age; transmitted by female *Anopheles* mosquito bite and, occasionally, congenitally, by blood transfusion (most frequently *Plasmodium malariae*) and by syringes (especially in drug addicts); variable incubation period (not < 7 d); greatly increases risk of HIV infection and death from AIDS

Agents: 73% *Plasmodium vivax*, 22% *Plasmodium falciparum*, 3% *Plasmodium ovale*, 2% *Plasmodium malariae*, 0.4% mixed; malaria due to simian plasmodia—*Plasmodium brasilianum*, *Plasmodium cynomolgi*, *Plasmodium inui*, *Plasmodium knowlesi*, *Plasmodium simium*—is very rare, may be acquired in nature or the laboratory, and is of moderate severity

Diagnosis: fever, chills, splenomegaly, decreased consciousness; sometimes dehydration, non-bloody diarrhoea, vomiting, jaundice, headache, muscle pains, anorexia; geographic history, transfusion or i.v. drug addict; Giemsa or Romanowski stain of thick and thin blood smears (3 in 48-72 h); indirect immunofluorescence when clinical diagnosis consistent with malaria but parasite not detected in thick blood films; dipstick antigen tests accurate when used by health professionals but not when used by travellers; indirect hemagglutination (experimental), immunodiffusion, ELISA (antibody); hyperbilirubinemia (total bilirubin 9.4 mg/dL), moderately elevated SGPT (15-56 U/mL) and SGOT, blood urea nitrogen 101 mg/dL, creatinine 6.8 mg/dL, anemia (hematocrit 24%, hemoglobin 8.3 g, erythrocyte count decreased), thrombocytopenia (platelets 180,000/μL)

Congenital: fever in 100%, splenomegaly in 93%, irritability in 85%, hepatomegaly in 84%, icterus in 79%

Vivax Malaria (Benign Tertian Malaria, Tertian Ague, Vivax Fever): usually non-fatal; incubation period 12-18 d; fever, headache, myalgia, malaise, nausea; after some time, paroxysms of fever and chills, ending in profuse sweating tend to occur every other day; tendency to relapse; sometimes associated with anemia, hepatomegaly and nonspecific hepatitis; occasionally complicated by spontaneous splenic rupture

Falciparum Malaria (Acute Pernicious Fever, Aestivo-Autumnal Fever, Aestivo-Autumnal Malaria, Algid Malaria (Gastrointestinal Symptoms Predominate), Chagues Fever, Continued Malarial Fever, Falciparum Fever, Malignant Tertian Fever, Malignant Tertian Malaria, Pernicious Intermittent Fever, Pernicious Malaria, Plasmodium Falciparum Malaria, Quotidian Malaria, Subtertian Fever, Subtertian Malaria Fever, Subtertian Malignant Tertian Malaria, Tertian

Malignant Malaria, Tropical Malaria): severe and, in nonimmune persons, rapidly fulminating; incubation period 8-15 d; high fever, chills, headache, myalgia, rapid pulse rate, splenomegaly, sometimes delirium; often a high level of parasitemia (to 72%) and capillary obstruction; initial fever may last several days, with some remissions; after initial illness, periodic pattern of paroxysms, with fever and chills, usually lasting 12-24 h and tending to be repeated every 48 h; coma, excessive destruction of erythrocytes, convulsions and heart failure may lead to death; the disease may produce very serious complications (cerebral malaria, hemoglobinuric falciparum malaria) and neurologic sequelae (memory impairment and diffuse white matter damage on magnetic resonance imaging)

Ovale Malaria (Ovale Tertian Malaria, Plasmodium Ovale Fever): relatively mild; incubation period 12-18 d; clinical manifestations similar to those of vivax malaria but paroxysms of fever and chills less severe; after initial stage, paroxysms tend to occur every other day; recovery often spontaneous; relapses not unusual

Malariae Malaria (Quartan Malaria, Quartan Ague, Quartan Fever): incubation period 20-40 d; clinical manifestations similar to those of vivax malaria but paroxysms of fever and chills commonly occur at intervals of 3 d; recovery often spontaneous but tendency for recrudescences to occur over many years; children may develop malarial nephropathy

Differential Diagnosis: fever and chills can suggest acute viral or bacterial infection; jaundice, anemia and splenomegaly other causes of hemolytic anaemia; leucopoenia and thrombocytopenia hematolgic malignancy, other severe infections; proteinuria and edema other causes of nephrotic syndrome; acute renal failure other causes of acute renal failure; hepatosplenomegaly and lymphocytic infiltration of hepatic sinusoids lymphoma; altered mental status, seizures and coma viral or bacterial meningitis, encephalitis, Reye's syndrome; bilateral pulmonary infiltrates acute respiratory distress syndrome related to shock from various causes

Treatment:

Uncomplicated *Plasmodium falciparum*: artemether + lumefantrine (5-14 kg: 1 20 + 120 mg tablet; 15-24 kg: 2 tablets; 25-34 kg: 3 tablets; > 34 kg: 4 tablets) orally with fatty food at 0, 8, 24, 36, 48 and 60 h, quinine sulphate 10 mg/kg to 600 mg orally 8 hourly for 7 d + doxycycline 2.5 mg/kg orally 12 hourly for 7 d (not in pregnant or < 8 y) or clindamycin 5 mg/kg to 300 mg orally 8 hourly for 7 d (in pregnant and < 8 y)

Severe (Altered Consciousness, Jaundice, Oliguria, Severe Anemia, Hypoglycemia, Vomiting, Acidotic, Parasite Count > 100,000/mm^3 Or > 2% Erythrocytes Parasitised): artesunate 2.4 mg/kg i.v. immediately and repeated at 12 h and 24 h, then once daily until oral therapy possible, then as above; if parenteral artesunate not available, quinine dihydrochloride 20 mg/kg i.v. over 4 h or 7 mg/kg i.v. over 30 min then 10 mg/kg i.v. over 4 h, after 4 h 10 mg/kg i.v. over 4 h 8 hourly

Others: chloroquine phosphate 10 mg/kg base to 620 mg orally as a single dose initially, then 5 mg/kg to 310 mg at 6, 24 and 48 h (severe cases: 10 mg base/kg rate controlled i.v. infusion over 8 h, followed by 15 mg/kg over 24 h or 3.5 mg base/kg i.m. or s.c. every 6 h until patient can take oral drugs) then primaquine 0.5 mg/kg base to 30 mg orally daily with food or, if nausea, 0.25 mg/kg to 15 mg orally 12 hourly with food for 14 d (*Plasmodium vivax*) or 0.25 mg/kg to 15 mg orally daily with food for 14 d (*Plasmodium ovale*) (avoid in persons with G6PD deficiency or, in mild cases, administer 45 mg base orally weekly for 6 w; avoid during pregnancy; not required in congenital or transfusion)

Prophylaxis:

Areas Without Chloroquine Resistant *Plasmodium falciparum*: chloroquine phosphate 5 mg/kg base to 310 mg orally once a week 1 w before entering to 4 w after leaving area, hydroxychloroquine sulphate 5 mg/kg base to 310 mg once a week 2 w before entering to 4 w after leaving area; where chloroquine cannot be administered: proguanil hydrochloride (< 2 y: 50 mg; 2-6 y: 100 mg; 7-10 y: 150 mg; > 10 y: 200 mg) orally daily 1 d before entering to 4 w after leaving area, doxycycline 1 mg/kg to 100 mg (not < 8 y) orally daily 1 d before entering to 2 d after leaving area (short stay only), mefloquine 250 mg orally weekly

Areas With Chloroquine Resistant *Plasmodium falciparum*: atovaquone + proguanil (11-20 kg: 62.5 + 25 mg; 21-30 kg: 125 + 50 mg; 31-40 kg: 187.5 + 75 mg; > 40 kg: 250 + 100 mg) orally with fatty food daily 1-2 d before entering to 7 d after leaving area, doxycycline 2.5 mg/kg to 100 mg orally daily (not < 8 y) 2 d before entering to 4 w after leaving area, mefloquine (5-9 kg: 31.25 mg; 10-19 kg: 62.5 mg; 20-29 mg: 125 mg; 30-44 kg: 187.5 mg; > 44 kg: 250 mg) orally weekly 2-3 w before entering to 4 w after leaving area, proguanil (< 2 y: 50 mg; 2-6 y: 100 mg; 7-10 y: 150 mg; >10 y: 200 mg) orally daily 1 w before entering to 4 w after leaving area + chloroquine 5 mg base/kg to 310 mg base orally weekly 1 w before entering to 4 w after leaving area if others contraindicated or not tolerated

To Prevent Delayed Attacks of *Plasmodium vivax* and *Plasmodium ovale*: primaquine 0.3 mg/kg to 15 mg daily for 14 d or 0.9 mg/kg to 45 mg weekly for 8 w (tafenoquine may replace)

Personal Protective Measures: wear light coloured long-sleeved shirts and long trousers in the evening; apply insect repellent containing not more than 35% diethylmetatoluamide sparingly to exposed skin; at dusk, spray aerosolised 'knock down' insecticide (eg., containing pyrethrins) in living and sleeping areas; sleep in a screened or air conditioned room or use bed netting of small mesh and good quality that is not damaged and is, preferably, impregnated

with permethrin; use mosquito coils or electrically operated insecticide generators containing pyrethroids; avoid outside activities between dusk and dawn; avoid stagnant water; avoid perfume and aftershave

Prevention and Control: mosquito control, treatment of cases

MYOCARDITIS AND PERICARDITIS

Agents: *human coxsackievirus B2-B5* (myocarditis of the newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis; > 50% of all cases), *human coxsackievirus A*, *human echovirus 6, 19*, several arboviruses, *mumps virus* (in 0.04% of mumps cases; may be fatal or followed by endocardial fibroelastosis), *measles virus*, *influenza A virus*, *influenza B virus*, adenovirus (common in paediatric HIV infection), *human cytomegalovirus* (common in pediatric HIV infection), rubella, *human hepatitis A virus*, *hepatitis B virus*, *simplexvirus 3*, *rabies virus*, *Lassa virus*, *human parvovirus B19* (in infants and heart transplant recipients), *Epstein-Barr virus, Neisseria meningitidis* (4% of purulent pericarditis), *Haemophilus influenzae* (3% of purulent pericarditis), *Pseudomonas aeruginosa*, *Campylobacter jejuni*, *Staphylococcus aureus* (23% of purulent pericarditis), *Actinobacillus actinomycetemcomitans* (rare), group C *Streptococcus* (rare), *Yersinia enterocolitica*, Q fever, *Listeria monocytogenes* (cardiac transplantation and others), *Actinomyces* (rare), *Mycoplasma pneumoniae*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, Rocky Mountain spotted fever (in 5% of infections), *Corynebacterium diphtheriae* (toxic manifestation occurring 2 d - 1 mo after onset of, especially, pharyngeal diphtheria), *Mycobacterium tuberculosis*, *Streptococcus pneumoniae* (33% of purulent pericarditis), *Rickettsia helvetica*, *Haemophilus aphrophilus* (rare), *Streptococcus pyogenes* (11% of purulent pericarditis), other Gram negative organisms (19% of purulent pericarditis), anaerobes (2% of purulent pericarditis), *Candida* (cardiac surgery, impaired host defences, severe debilitating disease), *Aspergillus* (pericarditis in 4% of disseminated cases), *Trichinella spiralis* (rare)

Diagnosis: viral culture of throat swab, feces, myocardium; serology; immunofluorescent antibody test on impression smear of myocardium; PCR of endomyocardial biopsy; bacterial and fungal culture of pericardial fluid or pericardium; histology of pericardium; latex agglutination and counterimmunoelectrophoresis of serum and pericardial fluid; blood cultures; when hemorrhagic pericardial effusions of undetermined cause are determined, the heart and great vessels should be evaluated as potential sources of the hemorrhage

Human parvovirus B19: PCR; bone marrow biopsy (pure red cell aplasia, giant proerythroblasts, vacuolisation of cytoplasm and intranuclear inclusions in paltry surviving precursors)

Diphtheric Myocarditis: thready pulse, faint heart sounds, cardiac arrhythmia; cardiac failure may occur

Pericardial Actinomycosis: 68% dyspnoea, 68% pleural effusion, 63% tachypnoea, 63% cough, 58% hepatomegaly, 53% fever, 53% chest pain

Treatment:

Influenza Virus: i.v. ribavirin

Human parvovirus B19: human immunoglobulin 0.5-1 g/kg/d i.v. for 4-5 d, erythropoietin

Other Viruses: non-specific

Actinomyces: benzylpenicillin 12-20 MU/d i.v. for 4-6 w, then phenoxymethylpenicillin or amoxycillin 2-4 g/d orally for 6-12 mo; tetracycline or erythromycin ± rifampicin 300 mg/d; clindamycin; chloramphenicol; third generation cephalosporin

***Neisseria meningitidis,* Streptococci:** benzylpenicillin

Haemophilus influenzae*, *Listeria monocytogenes: ampicillin

Pseudomonas aeruginosa: azlocillin + tobramycin

Campylobacter jejuni: erythromycin

Staphylococcus aureus: vancomycin

Actinobacillus actinomycetemcomitans*, *Rickettsia: tetracycline, chloramphenicol

Coxiella burnetii: doxycycline, tetracycline, erythromycin, rifampicin

Yersinia enterocolitica: pefloxacin 400 mg twice daily + tobramycin 75 mg twice daily

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo) + prednisone 40-80 mg daily, decreasing over several weeks

Mycoplasma*, *Ureaplasma: tetracycline, erythromycin

Candida: amphotericin B + pericardiectomy

Aspergillus: itraconazole, amphotericin B

Trichinella spiralis: albendazole, mebendazole

Prophylaxis (*Neisseria meningitidis*) ceftriaxone 250 mg (child 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children)

CARDITIS

Agents: adenovirus, *human echovirus 7, 11, 30*, *poliovirus*, *Streptococcus pyogenes* (rheumatic fever; carditis due to host immune response and local cross-reactive antigen; < 200 cases/y in USA); highest incidence in 3-4 y group

Diagnosis:

Viral: isolation from infected tissue

Rheumatic Fever: carditis in 40-50% of cases, polyarthritis in 75%, chorea in 15%, erythema marginatum in 10%, subcutaneous nodules, previous rheumatic fever or rheumatic heart disease, arthralgia, fever; acute phase reactants; prolonged PR interval; heart murmurs (tend to be variable from day to day), cardiac enlargement, pericardial friction rub, tachycardia persisting during sleep, congestive cardiac failure; recent scarlet fever; anti-streptolysin O test (normal in ≈ 20% of early cases; peaks at 2-4 w; false positives due to activity of other substances neutralising hemolytic properties of streptolysin O (eg., serum β-lipoprotein in liver disease) and bacterial growth in serum specimens), anti-DNAse B test (consistently elevated; rises later than ASOT, peaks at 4-6 w and remains elevated longer than ASOT; magnitude of response may be suppressed by antimicrobial therapy; detergents, heavy metals, azide and other chemicals interfere with enzyme and colour reaction), anti-hyaluronidase, anti-streptozyme (almost all patients have levels > 200 U); culture of nasal and throat swabs and swab of impetiginous lesions

Treatment:

Viral: non-specific

Rheumatic Fever: benzathine penicillin 1.2 MU (child: 600 000 U) i.m. once as a single dose, phenoxymethylpenicillin 250 mg orally 8 hourly for 10 d, or erythromycin 250 mg orally 6 hourly (child: 40 mg/kg/d in 4 divided doses) for 10 d for initial attack, followed by continuous, long term (well into adulthood, perhaps life-long) benzathine penicillin 900 mg (< 20 kg: 450 mg) i.m. every 3-4 w, phenoxymethylpenicillin 250 mg orally 12 hourly, or erythromycin 250 mg orally 12 hourly or erythromcyin ethyl succinate 400 mg orally 12 hourly (penicillin hypersensitive); aspirin or non-steroidal anti-inflammatory drugs for synovitis/arthritis

ENDOCARDITIS: 4% of community acquired and 1% of nosocomial bacteremia; commonly associated with aortic regurgitation, mitral regurgitation, congenital aortic stenosis (bicuspid valve), prosthetic heart valves, tricuspid regurgitation, ventricular septal defects, patent ductus arteriosus, coarctation of the aorta, arteriovenous fistula; native valves in 76%

Agents: 31-46% oral streptococci (*Streptococcus milleri*, *Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus sanguis;* 25-27% in late, and 1-6% in early, infections in prosthetic valve patients; 10% in drug addicts; 19% in recurrent episodes; 18% in children), 16% anaerobic and microaerophilic Gram positive cocci, 10-32% *Staphylococcus aureus* (50-61% in drug addicts; 7-20% in early, and 11-15% in late, infections in prosthetic valve patients; 26% in recurrent episodes; cause of > 50% of cases of acute progressive infective endocarditis; more frequent in children (37% of cases) and in elderly; involves previously normal valves in ≈ 50% of cases; only cause of eustachian valve endocarditis; should be considered in any patient with staphylococcal bacteremia), 8-10 % enterococci (9% in late, and 3-4% in early, infections in prosthetic valve patients; 8% in drug addicts; 13% in recurrent episodes; 14% in bone marrow transplant recipients), 7-14% *equines* (associated with gastrointestinal lesion, especially colon carcinoma), 7-9% coagulase negative staphylococci (25-44% in prosthetic valve patients; 2% in drug addicts; 4% in recurrent episodes; 57% of cases in bone marrow transplant recipients; 12% in children), 7% Gram negative bacilli (*Pseudomonas* (3% of primary, and 4% of recurrent, episodes; *Pseudomonas aeruginosa* 14% of cases in drug addicts, 4% in children; *Pseudomonas alcaligenes* in bone marrow transplant recipients; *Burkholderia cepacia* 0.6% in children, associated with cystic fibrosis and chronic granulomatous disease, also in injection heroin abusers and patients with prosthetic heart valves), *Stenotrophomonas maltophilia* (associated with i.v. drug abuse and prosthetic valve surgery), *Haemophilus* (1% of primary, and 2% of recurrent, episodes; oral source; *Haemophilus influenzae* 0.6% in children; *Haemophilus aphrophilus* 0.6% in children; *Haemophilus parainfluenzae* 2% in children; *Haemophilus paraphrophilus*, *Aggregatibacter segnis*, *Haemophilus aegytius)*; *Kingella kingae* (5-20% of early, and 10-18% of late, infections in prosthetic valve patients; also native valves); *Prevotella melaninogenica* (oral source; polymicrobial), *Fusobacterium nucleatum* and *Fusobacterium necrophorum* (oral source), *Bacteroides*, *Brucella* (1% in children), *Cardiobacterium hominis* (oral source), *Actinobacillus actinomycetemcomitans* (oral source; associated with periodontitis and prosthetic valves), *Eikenella corrodens* (oral source), *Yersinia enterocolitica*, *Flavobacterium meningosepticum* (in rheumatic heart disease, open heart surgery and i.v. drug abuse), *Salmonella enterica subsp enteric* serotype *paratyphi C*, *Salmonella choleraesuis* and other *Salmonella* (54% AIDS patients, 34% oncology patients; also elderly with previous valvular heart disease; 70% fatality rate), *Coxiella burnetii* (0.6% in children; 17% chronic; 37% mortality), *Chlamydophila pneumoniae*, *Legionella* (prosthetic valves), *Streptobacillus moniliformis* (rare complication of rat bite fever), *Alcaligenes* (0.6% in children), *Achromobacter xylosoxydans xylooxydans* (catheter related in bone marrow transplant recipients), *Campylobacter fetus* subsp *fetus* (0.6% in children), *Escherichia coli* (3% in children; 47% previous heart disease; 47% from urinary tract; 47% nosocomial; 84% new or changing murmur; 58% mitral valve; case-fatality rate 53%), *Proteus mirabilis* (0.6% in children), other Enterobacteriaceae, *Suttonella*

indologenes (rare), *Moraxella osloensis, Acinetobacter calcoaceticus, Capnocytophaga canimorsus, Agrobacterium tumefaciens* (prosthetic valve), *Bordetella bronchiseptica*, *Aeromonas*, *Tropheryma whipplei*), 3% *Streptococcus pyogenes* (1% in recurrent episodes; 0.6% in children) and other β-haemolytic streptococci (including *Streptococcus agalactiae* (postpartum and postabortion, diabetics and alcoholics; 83% affecting native valve; case-fatality rate 44-47% overall, 100% if affecting prosthetic valve; 2% in recurrent episodes; 1% in children), Group C *Streptococcus* (*Streptococcus zooepidemicus*, *Streptococcus equisimilis*, rarely *Streptococcus equi*) and *Streptococcus canis* (rare)), 3% other streptococci (including *Streptococcus pneumoniae*), 2% *Corynebacterium* (especially *Corynebacterium jeikeium* (6-8% in early, and 2-4% in late, infections in prosthetic valve patients; 2% in drug addicts; 14% in bone marrow transplant recipients); *Corynebacterium xerosis* (0.6% in children; also in i.v. drug abusers with AIDS); *Corynebacterium pseudodiphtheriticum* (1% in children); non-toxigenic strains of *Corynebacterium diphtheriae*), 2% fungi (10% in drug addicts; 6-10% in early, and 2-6% in late, infections in prosthetic valve patients; mainly *Candida* (3% in recurrent episodes; 14% in bone marrow transplant recipients; *Candida parapsilosis* in i.v. drug addicts, invasive procedure, prosthetic devices, hyperalimentation, 0.6% in children; also *Cryptococcus neoformans*, *Histoplasma capsulatum*, *Chrysosporium* (associated with prostheses), *Drechslera* (post surgery for ventricular septal defect), *Aspergillus* (coronary artery surgery, liver transplantation); *Aspergillus flavus* 0.6% in children; *Aspergillus fumigatus* 0.6% in children), *Pseudallescheria boydii* (in prosthetic valves and in AIDS); rarely, *Curvularia lunata*), *Neisseria gonorrhoeae* (0.6% in children), *Erysipelothrix rhusiopathiae* (animal contact (slaughterhouse workers, fish handlers, butchers, farmers), alcohol abuse; case-fatality rate 38%), *Listeria monocytogenes* (complicating rheumatic fever or prosthetic heart valve, malignancy, immunosuppressed, following coronary artery bypass surgery; case-fatality rate 29%), *Rothia dentocariosa* (rare; i.v. drug abuse, poor dentition, congenital heart disease), *Mycobacterium chelonae* and *Mycobacterium fortuitum* (infecting prosthetic valves), *Lactobacillus* (very rare; oral source; usually patient with preexisting structural heart disease and recent dental infection or manipulation; mortality 5-25%), *Propionibacterium acnes* (oral source), *Veillonella parvula* (oral source; polymicrobial; rare), *Neisseria mucosa* (i.v. drug abuser; oral source), *Neisseria sicca*, *Neisseria subflava* (i.v. drug abusers with AIDS; oral source), *Neisseria flavescens* (i.v. drug abusers with AIDS), *Neisseria elongata, Oerskovia* (prosthetic valves), *Rothia mucilaginosa* (i.v. drug abusers, cardiac valve disease, vascular catheter, immunocompromised), *Enterococcus faecalis* (5% in children), *Micrococcus* (0.6% in children), *Bacillus cereus* (infrequent; valvular heart disease, i.v. drug abuse), *Acinetobacter* (rare), *Actinomyces* (rare), *Staphylococcus lugdunensis* (mainly community acquired, usually preexisting cardiac abnormality), *Peptostreptococcus magnus* (oral source), *Aerococcus viridans* (rare), *Bartonella, Mycoplasma hominis, Pasteurella dagmatis, Yersinia enterocolitics, Cunninghamella bertholletiae* (after kidney transplantation)

Diagnosis: prior heart disease in 60-80%; constitutional symptoms in 90-100%, fever in 85-100%, heart murmur in 60-95%, emboli in 33%, petechiae in 30-79%, microscopic hematuria in 30-50%, heart failure in 25-66%, splenomegaly in 23-60%, mycotic aneurism in 2-11%; 2-dimensional echocardiogram (abnormalities in 34%; vegetations usual in *Streptococcus viridans* infections and in 40% of Q fever endocarditis; right bundle branch block in gonococcal endocarditis), colour flow Doppler technology, transesophageal echocardiography; blood cultures (take 3 sets before starting therapy; positive in 80%; bone marrow culture and combined arterial/venous blood cultures if negative); complement fixation tests, microagglutination tests, indirect fluorescent antibody titre, ELISA (antibody), counterimmunoelectrophoresis of serum; histology and PCR of diseased valves; elevated erythrocyte sedimentation rate in 90-100% of cases; total hemolytic complement decreased when glomerulonephritis also present; white cell count elevated in 20-66% of cases; rheumatoid factor in 50-80% of bacterial cases; anemia in 40-80%

Staphylococcus aureus: right-sided usually involves tricuspid valve, occurs mainly in young users of injecting drugs but also as nosocomial infection associated with indwelling central venous catheters, and presents acutely with fever, chills, leucocytosis, bacteremia and with focal, rounded, sometimes cavitary infiltrates on chest radiograph; left-sided usually associated with community acquired bacteremia of unknown origin and carries high mortality

Q Fever: work in abattoir or on farm; usually preceded by atypical pneumonia and acute hepatitis; fever in 67% of cases, cardiac failure in 66%, hepatosplenomegaly in 57%, increased γ-globulin in 94%, increased ESR in 89%, increased SGOT in 83%, increased alkaline phosphatase in 80%, thrombocytopenia in 67%; serology (complement fixation test, indirect immunofluorescence); isolation from cardiac valves; liver biopsy

Erysipelothrix rhusiopathiae: erysipeloid present in 36%

***Brucella*:** acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Differential Diagnosis: acute rheumatic fever, marasmic endocarditis, systemic lupus erythematosus, vasculitis, atrial myxoma, atrial thrombus, hpyernephroma, carcinoid, *human cytomegalovirus* in patients recently having valve replacement

Treatment: benzylpenicillin 45 mg/kg to 1.8 g i.v 4 hourly + di(flu)cloxacillin 50 mg/kg to 2 g i.v. 4 hourly + gentamicin 4-6 mg/kg (child: < 10 y: 7.5 mg/kg; ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function)

Nosocomial, Immediate Penicillin Hypersensitive, Patients with Prosthetic Valves, Community-associated Methicillin Resistant *Staphylococcus aureus* Suspected: vancomycin 25 mg/kg to 1

g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly slowly over 60 min (monitor blood levels and adjust dose to trough 10-20 mg/L) + gentamicin 4-6 mg/kg (child: < 10y: 7.5 mg/kg; ≥ 10 y: 6 mg/kg) i.v. daily (monitor blood levels and adjust dose to trough 0.5-1 mg/L) + early removal and replacement of prosthesis

Streptococci with Benzylpenicillin MIC ≤ 0.12 mg/L:

Uncomplicated: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 14 d + gentamicin 1 mg/kg i.v. 8 hourly for 14 d (monitor plasma levels); benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 4 w

Complicated (Large Vegetation, Multiple Emboli, Symptoms > 3 mo, Secondary Sepsis): benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 4 w + gentamicin 1 mg/kg i.v. 8 hourly for 14 d (monitor plasma levels)

Streptococci with Benzylpenicillin MIC > 0.12 & ≤ 0.5 mg/L: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 4 w + gentamicin 1 mg/kg i.v. 8 hourly for 14 d (monitor palsma levels)

Streptococci with Benzylpenicillin MIC > 0.5 but < 4 mg/L, *Abiotrophia*, *Granulicatella*, Susceptible Enterococci, *Rothia dentocariosa*, Culture Negative Where Q Fever or Fungal Infection Not suspected: gentamicin 1 mg/kg i.v. 8 hourly for 6 w (monitor plasma levels and adjust dose to trough 0.5-1 mg/L) or (in elderly) netilmicin 1 mg/kg i.v. 8 hourly for 14 d + benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly for 6 w or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 6 w

Streptococci With Benzylpenicillin MIC > 4 mg/L, Penicillin Hypersensitive: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly slowly over 60 min (monitor blood levels and adjust dose to trough 10-20 mg/L) for 4-6 w + gentamicin 1 mg/kg i.v. 8 hourly (monitor blood levels and adjust dose to trough 0.5-1 mg/L for 4-6 w or (for elderly) netilmicin 1 mg/kg i.v. 8 hourly

Vancomycin Resistant Enterococci: linezolid, quinupristin-dalfopristin

***Neisseria*, *Haemophilus parainfluenzae, Haemophilus aprophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae*:** cefotaxime 50 mg/kg to 2 g i.v. 8 hourly for 4 w or ceftriaxone 50 mg/kg to 2 g i.v. daily for 4 w

***Fusobacterium*, *Prevotella*:** metronidazole, tetracycline ± lincomycin

***Brucella*:** streptomycin 1 g twice a day i.m. for 30 d + doxycycline 100 mg twice a day orally for 90 d + rifampicin 900 mg/d orally for 90 d + cotrimoxazole 5/25 mg/kg/d in 4 equally divided doses for 90 d, or oxytetracycline 500 mg orally 6 hourly for 12 w + gentamicin 120 mg i.m. 8 hourly for 4 w; + surgery (valvular replacement with biprosthetic valve)

***Salmonella*:** ampicillin 2 g i.v. 6 hourly for 6 w (child: 150-200 mg/kg i.v. daily in divided doses) + gentamicin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly (trough < 1.5 mg/L) for 6 w; ciprofloxacin, ceftriaxone, cefotaxime

Streptobacillus moniliformis, Actinomyces: benzylpenicillin 12-20 MU (neonates: 500,000-1 MU; child: 200,000-400,000 U/kg) i.v. daily in divided doses for 30 d

***Legionella*:** erythromycin 4 g i.v. daily in divided doses for 2-6 mo (consider change to 2 g orally daily after 2 mo) + rifampicin 600 mg orally for up to 14 mo; ciprofloxacin 600 mg i.v. daily in divided doses + rifampicin 1200 mg orally daily for 10 w

***Flavobacterium meningosepticum*:** sulphadiazine + rifampicin

***Pseudomonas aeruginosa*:** azlocillin 3 g i.v 4 hourly (child: 225 mg/kg i.v. daily in 3 divided doses) + amikacin 5 mg/kg i.v. 8 hourly

Burkholderia cepacia: cotrimoxazole ± polymyxin B + valvectomy or valve replacement

***Stenotrophomonas maltophilia*:** cotrimoxazole + ticarcillin + rifampicin

Escherichia coli: ceftriaxone ± aminoglycoside

Acinetobacter: polymyxin, ampicillin-sulbactam, imipenem, cefperazone-sulbactam

***Alcaligenes*:** imipenem

***Bartonella*:** doxycycline 2.5 mg/kg to 100 mg doxycycline 12 hourly for 6 w (not < 8 y) + gentamicin 1 mg/kg i.v. 8 hourly for 14 d or rifampicin 7.5 mg/kg to 300 mg orally 12 hourly for 14 d

Other Gram Negative Bacilli: gentamicin 5 mg/kg i.v. daily (trough < 1.5 mg/L) for 6 w or tobramycin 5 mg/kg daily for 6 w + ticarcillin for 4-6 w; early consultation with cardiovascular surgeon and clinical microbiologist or infectious diseases physician

Staphylococci: early surgery +

Left-sided:

Methicillin Susceptible: di/flucloxacillin 50 mg/kg to 2 g i.v. 4 hourly for 4-6 w

Methicillin Resistant: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly over 60 min for 4-6 w (monitor blood levels and adjust dose to trough 10-20 mg/L)

Tricuspid Valve: di/flucloxacillin 50 mg/kg to 2 g i.v. 4 hourly for 4 w

***Bacillus*:** clindamycin

***Lactobacillus*:** benzylpenicillin 15-20 MU (neonates: 500,000-1 MU; older children: 200,000-400,000 U/kg) i.v. daily in divided doses for 2 w ± gentamicin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly (trough <1.5 mg/L)

***Erysipelothrix rhusiopathiae*:** benzylpenicillin 12-20 MU/d i.v. for 4-6 w

***Corynebacterium jeikeium*:** vancomycin

Other *Corynebacterium*: penicillin ± aminoglycoside; vancomycin

Listeria monocytogenes: ampicillin or penicillin, cotrimoxazole

***Mycobacterium chelonae*, *Mycobacterium fortuitum*:** 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

***Coxiella burnetii*:** tetracycline 2 g orally daily in divided doses + clindamycin 600 mg i.v. 8 hourly; rifampicin 10 mg/kg to 600 mg orally daily + cotrimoxazole 2/10 mg/kg to 160/800 mg orally twice daily; doxycycline + hydroxychloroquine for 2 y in chronic cases

Pasteurella: penicillin, ampicillin, mezlocillin, piperacillin, cefuroxime, ceftriaxone, cefotaxime

Fungi: valve replacement essential to management; amphotericin B (increase to 1 mg/kg daily; total dose of 2 g or more) + ketoconazole; fluconazole

Surgery where appropriate therapy fails to control infection or refractory congestive cardiac failure occurs.

Test of Progress: fall in circulating immune complexes levels

Prophylaxis: required with most congenital cardiac defects, previous endocarditis, hypertrophic cardiomyopathy, mitral valve prolapse with regurgitation, prosthetic valve, rheumatic and other acquired valvular dysfunction, surgically constructed systemic-pulmonary shunts or conduits

Bronchoscopy with Rigid Bronchoscope, Dental Procedures (Dental Extractions, Surgical Drainage of Dental Abscess, Maxillary or Mandibular Osteotomies, Surgical Repair or Fixation of Fractured Jaw, Periodontal Procedures (Including Probing, Scaling, Root Planing, Surgery), Dental Implant Placement and Reimplantation of Avulsed Teeth, Endodontic (Root Canal) Instrumentation or Surgery Only Beyond the Apex, Subgingival Placement of Antibiotic Fibres or Strips, Initial Placement of Orthodontic Bands (but not Brackets), Intraligamentary Local Anesthetic Injections, Prophylactic Cleaning of Teeth or Implants Where Bleeding is Anticipated), Surgical Procedures Breaking Respiratory Mucosa, Tonsillectomy and/or Adenoidectomy: 0.5% chlorhexidine applied to gingival margin before local anasthesia for dental surgery; amoxycillin 50 mg/kg to 2 g orally as a single dose 1 h before procedure; amoxy(ampi)cillin 50 mg/kg to 2 g i.v. just before procedure or i.m. 30 min before procedure

Penicillin Hypersensitive, On Long-term Penicillin or Having Taken β-lactam Antibiotic More Than Once in Previous Month: clindamycin 15 mg/kg to 600 mg orally single dose 1 h before procedure or i.v. over at least 20 min, ending just before procedure commences; lincomycin 15 mg/kg to 600 mg i.v. over at least 1 h, ending just before procedure commences; vancomycin 25 mg/kg to 1.5 g i.v. (child 30 mg/kg to 1.5 g) over at least 1 h, ending just before procedure commences; teicoplanin 10 mg/kg to 400 mg i.v. just before procedure or i.m. 30 min before procedue; cephalexin 50 mg/kg to 2 g orally 1 h before procedure (not those on long-term penicillin or having taken related beta-lactam > once in previous month or with immediate penicillin hyprsensitivity)

Endoscopic Retrograde Cholangiography, Biliary Tract Surgery, Esophageal Dilatation, Sclerotherapy for Esophageal Varices, Surgical Procedures Breaking Intestinal Mucosa (Except Endoscopy, Biopsy, Percutaneous Endoscopic Gastrostomy), Prostatic Surgery, Transrectal Prostatic Biopsy, Cystoscopy, Urethral Catheterisation or Urinary Tract Surgery in Presence of Urinary Tract Infection, Urethral Dilatation and Curettage, Therapeutic Abortion, Sterilisation Procedures or Insertion or Removal of Intrauterine Contraceptive Device in the Presence of Infection, Vaginal Delivery in Presence of Infection or Prolonged Labour: (amoxy)ampicillin 50 mg/kg to 2 g i.v. just before procedure or i.m. 30 minutes before procedure then 25 mg/kg to 1 g i.v. i.m. or orally 6 h later + gentamicin 2 mg/kg (child: 2.5 mg/kg) i.v. just before procedure or i.m. 30 min before procedure

Penicillin Hypersensitive: vancomycin 25 mg/kg (< 12 y: 30 mg/kg) to 1.5 g i.v. over at least 1 h, ending just before procedure, teicoplanin 10 mg/kg to 400 mg i.v. just before procedure

Patients With Prosthetic Valves Or Previous Endocarditis Undergoing Skin Biopsy: di(flu)cloxacillin 25 mg/kg to maximum 1 g i.v. just before procedure commences or i.m. 30 min before procedure + gentamicin 2 mg/kg (child: 2.5 mg/kg) i.v. just before procedure commences or i.m. 30 min before procedure

If Parenteral Thrapy Impractical: di(flu)cloxacillin 25 mg/kg to maximum 1 g orally 1 h before procedure commences, then 25 mg/kg to maximum 1 g orally 6 h later

Penicillin Hypersensitive: vancomycin 20 mg/kg to maximum 1 g i.v. slowly over 60 min + gentamicin as above

VASCULAR GRAFT INFECTION

Agents: 33% *Staphylococcus aureus*, 16% *Escherichia coli*, 12 % *Staphylococcus epidermidis,* 11% streptococci, 8% *Proteus*, 7% other aerobic Gram negative bacilli, 6% other bacteria (including *Listeria monocytogenes*), 1% *Candida*, rarely *Aspergillus*

Diagnosis: culture of surgical specimen, blood cultures

***Aspergillus*:** persistent back pain, fever, arterial embolusation

Treatment: surgery + vancomycin 20 mg/kg to 1 g i.v. slowly 12 hourly (trough 10-20 mg/L) + cefotaxime 50 mg/kg to 2 g i.v. 8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. daily

MYCOTIC ANEURISM: present in 2-11% of endocarditis cases, also due to direct arterial infection

Agents: 18-66% *Salmonella*, 16-44% *Staphylococcus aureus*; *Streptococcus pneumoniae*, other streptococci, enterococci, *Mycobacterium tuberculosis*, *Yersinia enterocolitica*, *Proteus*, *Klebsiella*, *Enterobacter*, *Campylobacter fetus* subsp *fetus*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Listeria monocytogenes*, *Escherichia coli, Haemophilus influenzae, Aspergillus*

Diagnosis: CT scan; aortography; blood cultures; smears and cultures of sputum, urine, bone marrow, surgical specimens

Treatment: surgery + vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. slowly 12 hourly (monitor blood levels and adjust dose to trough 10-20 mg/L) + cefotaxime 50 mg/kg to 2 g i.v. 8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. daily

FALSE ANEURISM: common in i.v. drug addicts

Agents: 83% *Staphylococcus aureus*, 39% polymicrobial, 22% streptococci, 20% anaerobes, 12% aerobic Gram negative bacilli

Diagnosis: computed tomography (sensitivity 100%), arteriography (sensitivity 96%), digital subtraction angiography (sensitivity 92%); blood cultures, culture of surgical material

Treatment: resection + appropriate antimicrobial

THROMBOPHLEBITIS: rarely affects CNS; although 33% of intravenous catheters give positive cultures, only 3% are associated with sepsis; development of infection in intravenous catheters is related to patient being already septic, transient bacteremia from another source, irrigating or otherwise manipulating an occluded, leaking or infiltrated catheter, contaminated fluid being administered, total parenteral nutrition, burned patient, length of time catheter remains in place, cancer patient, corticosteroids and/or other immunosuppressive therapy, plastic cannulas (as opposed to steel), intravenous therapy in lower extremity

Agents: 40% *Klebsiella-Enterobacter*, 20% *Providencia*, 20% *Proteus*, 12% *Serratia marcescens,* 12% *Staphylococcus aureus* (associated with local trauma), 8% *Pseudomonas aeruginosa*, 8% *Escherichia coli*, 8% *Candida*; *Campylobacter fetus* subsp *fetus*, halophile *Vibrio*, *Aeromonas*, *Corynebacterium striatum* (rare; associated with central venous catheters), *Staphylococcus epidermidis*

Diagnosis: culture of infected material; blood cultures

Treatment: dependent on agent

Prevention: intravenous catheters should be used only when less dangerous methods are not possible; catheter must be inspected daily; three-way stopcocks should be avoided if possible or, if not, should at least be changed at least every 24 hours, because they provide a portal of entry for bacteria or fungi; forced irrigation should be avoided because of possibility of thromboembolism; in placing an intravenous catheter, prepare area with antiseptic solution (chlorhexidine), use sterile drapes and gloves, apply 2% chlorhexidine ointment to the site after insertion, anchor catheter securely, apply sterile dry gauze (not transparent occlusive) dressing, 'date' catheter, use antiseptic/antibiotic impregnated short-term central venous catheter if rate of infection is high despite adherence to other strategies

ARTERITIS

Agent: *Pythium* (in thalassemic farmers), *Aspergillus*

Diagnosis: histology and culture of surgical material

Treatment:

Pythium: aggressive surgery + i.v. sodium iodide

***Aspergillus*:** surgery + amphotericin B

BACILLARY ANGIOMATOSIS: largely in immunocompromised patients, particularly AIDS

Agent: *Bartonella henselae*, *Bartonella quintana*

Diagnosis: Warthin-Starry stain of biopsy

Treatment: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 3-4 mo (not < 8 y), erythromycin 10 mg/kg to 500 mg orally 6 hourly for 3-4 mo, erythromycin ethyl succinate 20 mg/kg to 800 mg orally 6 hourly fo 3-4 mo

Chapter 10

Infections of the Reticuloendothelial System

Bone Marrow Infections

Agents: *Brucella, Salmonella typhi, Mycobacterium, Histoplasma capsulatum*

Diagnosis: hematological examination of bone marrow (infection causes an increased M/E ratio; in chronic infection, there is a myeloid hyperplasia and increased plasma cells; *Mycobacterium kansasii* causes a severe hypoplasia of hematopoietic cells); Gram stain, Ziehl-Neelsen stain, culture of bone marrow in biphasic medium for 3 w, aerobic and anaerobic bacterial cultures and fungal cultures at 25°C and 35°C on solid media, and culture for mycobacteria as indicated and quantity of specimen allows

***Brucella*:** acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Treatment:

***Brucella*:** doxycycline 100 mg orally twice a day + rifampicin 600 mg orally 4 times a day or streptomycin 1 g i.m. 4 times a day fro 45 d, ciprofloxacin 500 mg orally twice a day + rifmapicin 600 mg orally twice a day for 30 d

***Salmonella typhi*:** chloramphenicol, cotrimoxazole

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Other Mycobacteria: ethionamide, cycloserine, viomycin, ethambutol

***Histoplasma capsulatum*:** amphotericin B, flucytosine, ketoconazole

Ehrlichiosis

Agent: *Ehrlichia canis, Ehrlichia chaffeensis* and *Ehrlichia sennetsu* (monocytic; tick vector—*Dermacentor variabilis* and *Amblyomma americanum* in Southern and Eastern USA), *Ehrlichia ewingii* and *Anoplasma phagocytophilum* (granulocytic; tick vector—*Amblyoma americanum* and *Ixodes persulcatus*)

Diagnosis: incubation period < 3 w; fever, malaise, headache, nausea, vomiting, anorexia, myalgia, arthralgia, chills, sweating, cough, diarrhoea, abdominal pain, thrombocytopenia, leucocytopenia, increased liver enzyme levels; maculopapular rash (rare in granulocytic); encephalopathy, pulmonary complication (respiratory failure, acute respiratory distress, pharyngitis; pulmonary infiltrates, pulmonary edema on chest X-ray) may occur in monocytic (may evolve with severe multiorgan failure); disseminated intravascular coagulation, meningitis, gastrointestinal bleeding and renal failure also occur; immunohistologic examination of acute phase bone marrow and liver biopsy; PCR (positive in 71%); morulae in Wright-Giemsa stained peripheral or buffy coat smears (positive in 61%); thrombocytopenia and leucopenia in 49%

Treatment: doxycycline

Hepatitis

Agents:

Prenatal: *human cytomegalovirus*, *rubella virus*, *simplexvirus*, *human coxsackievirus B*, *simplexvirus 3*, *Listeria monocytogenes* (intrauterine infection with septicemia; mortality high), *Treponema pallidum subsp pallidum*

Neonatal: *simplexvirus*, *human cytomegalovirus*, *human echovirus*, *Reovirus*, *measles virus* (fatal in children with leukemia), *Listeria monocytogenes* (acquired from environment; majority recover)

Pediatric: *simplexvirus 3, human parvovirus B19*

Adult: hepatitis A (infective hepatitis; acute viral disease of worldwide occurrence, particularly in Third World areas; global incidence 600,000 - 3M/y ; ≈ 2000 notified cases/y in Australia (≈ 27% in NSW; causes 3% of fever in returned travellers); incidence 13/100,000 in USA but 33% serological evidence of prior infection; 0.02% of new episodes of illness in UK; 80% of hepatitis in travellers; global mortality 2400-12,000/y; case-fatality rate 0.1-0.3% overall, 1.8% in > 50 y.o.; antibody positivity varies from 30% in Switzerland to ≈ 100% in Africa, Asia, Latin America, Mexico and South America; from shellfish from contaminated waters, raw produce, uncooked foods and cooked foods not reheated after contact with infected food handler; 50% no identified source, 12-26% household or sexual contact, 10% drug users and men who have sex with men; incubation period 15-50 d; duration of illness 2 w-3 mo), hepatitis B (serum hepatitis; ≈ 8000 notified cases/y

(52% in NSW) in Australia; global mortality rate 1-2M/y (tenth leading cause of death); case-fatality rate generally 1% but up to 67% in some outbreaks; prevalence of HBsAg varies from 0.2-0.5% in Australia up to 80% in Taiwan; very common in China, SE Asia, Subsaharan Africa, Pacific Islands and the Amazon Basin; 181,000 new cases/y, 1.25 M with chronic infection, and 5000 deaths from related cirrhosis or hepatocellular carcinoma in USA; low incidence in W Europe and Australia (≈ 300 notified cases/y (≈ 35% in Queensland)); carrier rate from 0.5% in USA and Canada and 1% in Australia to 5-15% of adults in developing nations; 385 M chronic carriers worldwide; Australian Aborigines have a very high carrier rate; becomes chronic in 90% infected at birth, 25-50% at 1-5 y; transmission by sex (40% heterosexual, 15% men having sex with men), blood and blood products, secretions (eg., saliva, semen), body fluids, contaminated needles/sharp instruments, human bites and intimate contact); incubation period 3-20 w; > 90% of HbeAg-positive mothers transmit to newborns through blood exposure at time of birth), hepatitis C (20% of all cases of acute hepatitis; injecting drug users (80% of cases), those who received a blood transfusion prior to 1992 (5-10%), hemodialysis patients, health care workers (prevalence 1-2%), hemophiliacs, those with transplants before 1992, intranasal cocaine users, those with body piercing, sexual contacts of infected persons, persons with multiple sex partners, individuals with tattoos, those sharing household items with infected individuals, those indulging in fisticuffs, patients of infected healthcare workers; also transmitted from infected mother to newborn (3-5% risk if mother has chronic infection); 15-35% clear infection spontaneously within 2-6 mo, 65-85% develop chronic infection, 5-20% with chronic infection progress to cirrhosis after 20 y (20% after 40 y; increased risk with alcohol consumption, HIV or hepatitis B coinfection, older age at time of infection, male), 3-5% with cirrhosis develop liver failure or hepatocellular carcinoma after 30-40 y; 170 M carriers worldwide; infection rates vary from < 0.5% in Scandinavian countries to 8-14% in Egypt; ≈ 200,000 infected in Australia with ≈ 134,000 having developed chronic infection, and ≈ 11,000 new infections/y); most common bloodborne infection and most common cause of liver transplant in USA (> 4 M infected; 30,000 new infections and 10,000 deaths annually; leading cause of death in HIV-infected patients in at least 1 US hospital), 8.9 M infected in Europe, 200 M worldwide), hepatitis D (delta hepatitis; superinfection of hepatitis B; transmitted in company with hepatitis B; 5% of HBsAg carriers infected worldwide; endemic in Russia, Romania, southern Italy, Africa and S America, rare in Australia (21 notified cases in 1999); associated with illicit drug usage and blood transfusions, less commonly sexually transmitted; chronic disease rare in acute cases but 70-80% chronic in HBsAg carriers; accelerates development of liver cancer; mortality 2-20%), hepatitis E (acute disease; enterically transmitted; water-borne epidemics in India, Nepal, Pakistan, Burma, former Soviet Union, Africa, Mexico, Middle East; 50% of non-A-C hepatitis in developing countries; endemic in Asia and South America; most common cause of acute sporadic hepatitis in Sudanese children; case-fatality rate up to 25% in pregnancy; 2 notified cases in Australia in 1999), hepatitis G (chronic; no known symptoms; prevalence 1-2% of blood donors, 30% of drug users, 10-30% of hepatitis C patients; transmitted by blood transfusion), *simplexvirus 1* (associated with pregnancy, thymic dysplasia, celiac disease, corticosteroid therapy, leukemias and lymphomas, severe burns, renal transplantation, AIDS; death within 1 w), *simplexvirus 3*, *human cytomegalovirus*, *Epstein-Barr virus*, several viral hemorrhagic fevers including *yellow fever virus* and *Lassa virus*, adenovirus, *human parvovirus B19*, *Staphylococcus aureus* (in toxic shock syndrome), *Listeria monocytogenes* (associated with debilitating and neoplastic diseases, immunosuppressive therapy, renal transplantation, cardiac prosthetic devices), *Escherichia coli*, *Salmonella typhi*, *Shigella*, *Pseudomonas pseudomallei*, *Brucella*, *Yersinia pseudotuberculosis, Campylobacter jejuni, Mycobacterium tuberculosis, Mycobacterium avium-intracellulare, Mycobacterium leprae* (in 90% of lepromatous cases, 20% of tuberculoid), *Treponema pallidum subsp pallidum*, *Leptospira*, Rocky Mountain spotted fever, Boutonneuse fever, Q fever (abattoir and farm workers), *Borrelia recurrentis*, *Actinomyces*, *Nocardia, Aspergillus, Mucor, Candida, Histoplasma*, *Leishmania*, *Plasmodium*, *Toxoplasma*, *Schistosoma, Echinococcus*, *Entamoeba histolytica* (hepatic amoebiasis (amoebic hepatitis); early stage of invasion of liver via intrahepatic portal vessels; results from intestinal amoebiasis; may be self-limiting or progress to a liver abscess), *Capillaria hepatica*, *Fasciola hepatica*; also alcohol, phenothiazine (chlorpromazine), anesthetics (halothane), antituberculous drugs (rifampicin, isoniazid, pyrazinamide), methyldopa, contraceptive pills, organic solvents (eg., carbon tetrachloride, 'glue')

Diagnosis: anorexia, malaise, extreme fatigue, right upper quadrant tenderness, nausea, vomiting, acute jaundice; epidemiological history; light-coloured stool, dark urine; computed tomography of abdomen (positive in 93% of cases of focal hepatic candidiasis), ultrasound; serology; Gram, Giemsa, Ziehl-Neelsen and silver-methenamine stains, bacterial, fungal and viral culture of biopsy; viral culture of throat swab, feces; increased urine urobilinogen, serum alanine aminotransferase > 2.5 times upper limit of normal; serum aldolase increased in viral hepatitis, less consistently in chronic hepatitis; serum β-glucuronidase increased in viral hepatitis; serum isocitrate dehydrogenase increased in viral hepatitis; serum iron and total iron-binding capacity increased in infectious hepatitis; serum sorbitol dehydrogenase increased in acute hepatitis; rheumatoid factor may be present; 80% of cases of chronic active hepatitis have anti-nuclear antibodies titre > 320; anti-smooth muscle antibody test +++ in hepatitis A and B, ++ in chronic active hepatitis, cryptogenic cirrhosis and primary biliary cirrhosis; cytoplasmic mitochondrial smooth muscle fluorescence in chronic active hepatitis and other liver disease; white cell count decreased in *simplexvirus* hepatitis

Hepatitis A: usually asymptomatic or unrecognised in children; in > 80% of adults, marked jaundice, diarrhoea, dark urine, flu-like symptoms (fever, headache, nausea, abdominal pain, fatigue, weakness, arthralgias, myalgias); may have clay coloured stools, skin rash and extreme aversion to tobacco smoke; ELISA tests for hepatitis A IgM antibody (persists

3-6 mo post infection) and total hepatitis A antibody (also antigen; capture IgA in protracted cases); immune adherence hemagglutination test for hepatitis A IgM antibody (not always reliable), seroconversion of hepatitis A IgG antibody; counterimmunoelectrophoresis; immunoelectron microscopy of stool; increase in ALT and AST; bilirubin normal or elevated

Hepatitis B: incubation period 4 w - 6 mo; may be asymptomatic, but usually fatigue, weakness, anorexia, nausea, fever, malaise and fullness or discomfort in right upper quadrant; jaundice in 20-50%; less frequently, hemorrhage due to diminished synthesis of prothrombin complex, altered mental status, Guillain-Barré syndrome, peripheral neuropathy, myokymia, neuropsychiatric dysfunction, red cell aplasia, thrombocytopenia, agranulocytosis, aplastic anemia, myocarditis, pericarditis, superficial/hemorrhagic gastritis, acute pancreatitis, renal failure, membranous glomerulonephritis, urticaria, papular acrodermatitis, arthralgia, vasculitis, pleural effusion; fatal fulminant hepatitis in 1% of acute infections; becomes chronic in 90% of infants, 60% of < 5 y.o. and 2-6% of adults; annual rate of development of cirrhosis 1-3% (5 y survival rate 30%); radioimmunoassay most sensitive; turkey erythrocyte passive haemagglutination test slightly less sensitive but simple, rapid and considerably less expensive; enzyme immunoassay (Auszyme I) 98% sensitivity and 99% specificity; hepatitis B surface antigen (HBsAg) indicates current infection but not necessarily infectivity; hepatitis B e antigen (HBeAg) indicates high infectivity in $HBsAg^+$ individual; anti-hepatitis B surface antibody (anti-HBs) indicates post-infection, immunity or (if IgM anti-HBc negative) chronic infection; anti-hepatitis B core antibody (anti-HBc; IgM diagnostic of acute infection); anti-hepatitis B e antibody (anti-HBe) indicates low infectivity in a $HBsAg^+$ individual

IgM HbcAb +ve = acute infection

HBsAb +ve HBcAb -ve HBV DNA -ve = hepatitis B immunisation

HBsAb +ve HBcAb +ve HBV DNA -ve = recovered from HBV

HBsAb +ve HBcAb ± HBV DNA < 10^3 copies = occult hepatitis B

HBsAb -ve HBcAb +ve HBeAb -ve HBsAg +ve = acute HBV or chronic hepatitis B

HbsAb -ve HbcAb +ve HbeAb -ve HbsAg -ve = occult hepatitis B

HBsAb -ve HBcAb +ve HBeAb +ve HBsAg +ve = healthy or inactive carrier

HbsAb -ve HbcAb +ve HbeAb +ve HbsAg -ve = occult hepatitis B

serum alanine aminotransferase > 10-20X normal in acute cases, 2-10X normal in chronic cases, < 2X normal in 'healthy' carrier state; total serum bilirubin 2.5-34.8 mg/dL; serum glutamic-oxaloacetic transaminase > 10X upper limit normal in all cases

Hepatitis C: incubation period > 21 d; generally asymptomatic in acute phase; malaise, weakness and anorexia in 25-35%; fatigue and malaise with advanced liver disease; arthritis in 23%, paresthesia in 17%, myalgia in 15%, pruritus in 15%, sicca symptoms of mouth and/or eyes in 11%, mixed cryoglobulins in 40%, low thyroxine level in 10%, antinuclear antibodies in 10%, anti-smooth muscle antibodies in 7% of chronic infections; glomerulonephritis, lichen planus, porphyria cutanea tarda, Raynaud's syndrome, systemic vasculitis, lymphoma, diabetes mellitus, corneal ulceration, autoimmune phenomena, uveitis, sialadenitis and peripheral neuropathy also occur; 1 case of acute disseminated encephalomyelitis reported; infection becomes chronic in 75-85%, with 60-70% having evidence of active liver disease and cirrhosis occurring in 20% of total within 20 y; test for anti-HCV by ELISA (false positives and negatives) and recombinant immunoblot assay (expensive and number of samples give indeterminate results) if positive, reverse transcriptase PCR for hepatitis C virus RNA (negative result does not necessarily exclude infection); genotyping; serum alkaline phosphatase 310 IU/mL, total serum bilirubin 2.6 mg/dL, serum glutamic-oxaloacetic transaminase > 100 U/mL; serum ALT and AST may be elevated in acute cases

Hepatitis D: incubation period 2-8 w; abrupt onset of signs and symptoms of hepatitis B; HbsAg +ve or IgM anti-HBc +ve + anti-HDV +ve

Hepatitis E: incubation period 2-9 w; immunoelectron microscopy of stool during incubation and early infection; IgM anti-HEV +ve; enzyme immunoassay, Western blot assay (IgM elevated 1 mo after infection, IgG after 6-8 w);

Q Fever: indirect fluorescent antibody titre, complement fixation test

Focal Hepatic Candidiasis: serum alkaline phosphatase increased in 92% of cases; total serum bilirubin increased in 36% of cases, direct in 33%

Parasites: complement fixation test, bentonite flocculation, indirect hemagglutination, latex agglutination, direct agglutination, indirect immunofluorescence, immunodiffusion, counterimmunoelectrophoresis

***Capillaria hepatica*:** acute or subacute hepatitis with high eosinophilia; may be splenomegaly, pneumonitis, fever, constipation and abdominal distension; case-fatality rate high; microscopy of biopsy or autopsy specimen for ova

***Fasciola hepatica*:** fever, pain in right hypochondrium, hepatomegaly, hypergammaglobulinemia, marked eosinophilia; ELISA

Treatment: ursodeoxycholic acid in chronic

Viruses: mainly non-specific; discontinue steroids

***Simplexvirus*:** famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

Hepatitis B (e Antigen Positive, Chronic Active Disease for ≥ 6 mo and on Liver Biopsy): lamivudine 100 mg orally daily until HbeAg is undetectable and replaced by anti-Hbe on 2 occasions at least 3 mo apart (may cause severe and fatal infection if resistance develops), interferon α-2 4.5-10x10^6 U s.c. 3 times a week for 6 mo or 5x10^6 units s.c. daily for 6 mo

Unresponsive: interferon α-2 9-10x10^6 U s.c. 3 times a week for further 6 mo; famiclovir; lamivudine

Renal Transplant Recipient: lamivudine, famciclovir

Liver Transplant Recipient: lamivudine 12 mo + long term hepatitis B immunoglobulins

Hepatitis C: pegylated interferon α-2b ± ribavirin (not if anemia, hemoglobinopathy, white blood cell count < 1500/mL, platelet count < 100,000/mL, pregnant or unable to practise contraception, decompensated cirrhosis, severe psychiatric illness, cardiovascular disease, seizure disorder or poorly controlled diabetes mellitus; low probability of effectiveness) ± amantadine for 6 mo if genotype 2 or 3, 1 y if genotype 1 or 4

Staphylococcus aureus: cloxacillin, penicillin

Listeria monocytogenes: penicillin, cotrimoxazole

Escherichia coli: gentamicin

Salmonella typhi: chloramphenicol, cotrimoxazole

Shigella: cotrimoxazole, ampicillin (not amoxycillin)

Burkholderia pseudomallei: cotrimoxazole + ceftazidime or meropenem or imipenem

Brucella: doxycycline + rifampicin or streptomycin, ciprofloxacin + rifampicin

Yersinia pseudotuberculosis: gentamicin, cefotaxime, doxycycline, ciprofloxacin

Campylobacter jejuni: erythromycin

Coxiella burnetii: tetracycline 500 mg orally 6 hourly for 14 d, doxycycline 100 mg orally 12 hourly for 14 d, rifampicin 600 mg (child: 7.5 mg/kg) orally daily, erythromycin 500 mg orally 6 hourly (child: 30 mg/kg/d in 4 divided doses) for 14 d

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Mycobacterium avium-intracellulare: ethambutol 15 mg/kg orally daily (not < 6 y) + clarithromycin 12.5 mg/g to 500 mg orally 12 hourly daily or azithromycin 10 mg/kg to 500 mg orally daily + rifampicin 10 mg/kg to 600 mg orally daily or rifabutin 5 mg/kg to 300 mg orally daily

Mycobacterium leprae: dapsone + isoniazid, sulphonamides

Treponema pallidum subsp pallidum: penicillin

Leptospira: oxytetracycline

Rickettsia: tetracycline, chloramphenicol

Borrelia recurrentis: penicillin, tetracycline, doxycycline (may be associated with Jarisch-Herxheimer reaction)

Actinomyces: penicillin ± streptomycin, tetracycline, erythromycin, third generation cephalosporin

Nocardia: sulphonamides, cotrimoxazole

Fungi: amphotericin B

Leishmania, Plasmodium: chloroquine, hydroxychloroquine sulphate, amodiaquine, mepacrine, quinine, primaquine, proguanil, pyrimethamine

Toxoplasma: sulphadiazine 1-1.5 g orally or i.v. 6 hourly for 3-6 w then 500 mg orally 6 hourly or 1 g orally 12 hourly + pyrimethamine 50-100 mg orally loading dose then 25-50 mg daily for 3-6 w (continue if necessary)

Sulphadiazine Hypersensitive: substitute clindamycin 600 mg orally or i.v. 6 hourly for 3-6 w (continue 8 hourly if necessary)

Schistosoma: praziquantel, niridazole, sodium stibogluconate

Echinococcus: thiabendazole

Entamoeba histolytica: chloroquine + emetine hydrochloride

Capillaria hepatica: no known treatment

Fasciola hepatica: bithionol

Prophylaxis:

Hepatitis A:

Postexposure: 0.02 mL/kg human immune globulin i.m. as a single dose within 2 w of exposure (close contact with persons having acute hepatitis A—household, sexual contacts, prisons, institutions for mentally retarded, day care centres; persons with repeated exposures within past 2 w to food prepared by IgM hepatitis A virus antibody positive handler handling high risk foods and with poor hygiene)

Preexposure: Travellers to Endemic Regions, People Attending Day Care Centres or Institutions Where Hepatitis A is Prevalent, Sewerage Workers, HIV Negative Homosexual Men, Food Handlers, Recipients of Blood Products, People With Significant Chronic Liver Disease, Illegal Drug Users: 2 doses of inactivated virosome vaccine provides 20 y protection (combined hepatitis A and B vaccine also available); care in handling feces, blood, other secretions and possibly contaminated objects

Hepatitis B: vaccine (low prevalence: health personnel, dialysis patients, institutionalised patients, drug addicts, male homosexuals, persons with history of sexually transmitted disease, persons who have had multiple sex partners, those who have had sex with injection drug user, household members, sex partners and drug-sharing partners of person with chronic infection, persons receiving clotting factor concentrates; high prevalence: all infants; months 0, 1, 2 and 12; inoculation in deltoid rather than buttock as gives better titres; 17% soreness at vaccination site, 15% fever, fatigue, headache, nausea; immunity 5 y but 30% require booster < 3 y after initial course; 2 types—plasma-derived and recombinant DNA; latter may require larger and repeated doses for hemodialysis patients and immunosuppressed patients; avoid in patients with risk of CNS disease) (combined hepatitis A and B vaccine also available), care in handling contaminated blood and secretions

Perinatal Exposure (Infants Born to HBsAg Positive Mothers): hepatitis B immune globulin (HBIG) 0.5 mL i.m. within 12 h of birth, followed by vaccine 0.5 mL i.m. at same times as HBIG or within 7 d, repeated at 1 and 6 mo

Percutaneous Exposure (Acute Exposure to HBsAg by Accidental Needle Stick or Mucosal Exposure):

Where Risk of Source of Infection Being Positive is High or Known to be HBsAg Positive: HBIG 0.06 mL/kg to maximum 5 mL i.m. as a single dose within 24 h, repeat at 1 mo or vaccine 0.5-1 mL at same time as HBIG or within 7 d, repeated at 1 and 6 mo if unvaccinated or partially vaccinated

Where Risk of Source of Infection Being Positive is Low or Source Unknown: vaccine only administered within 7 d of exposure; otherwise, no prophylaxis

Sexual Exposure (Sexual Contact of Persons with Acute Hepatitis B during Previous Month): HBIG 0.06 mL/kg to 5 mL maximum i.m. + hepatitis B vaccine within 14 d

Hepatitis C (Percutaneous Exposure): if source HCV antibody negative and unlikely to be in window period, none; otherwise, HCV RNA testing at 4-6 w and HCV antibodies and ALT at 4-6 mo; consider early therapy if seroconversion

***Mycobacterium avium* Complex in HIV/AIDS, CD4 < 50/μL:** azithromycin 1.2 g orally weekly, clarithromycin 500 mg orally 12 hourly, rifabutin 300 mg orally daily

***Toxoplasma gondii* in HIV/AIDS, CD4 < 200/μL:** cotrimoxazole 80/400 or 160/800 mg orally daily or 160/800 mg orally 3 times daily

Liver Carcinoma may be caused by hepatitis B virus transforming hepatic cell. Liver cancer is especially common in those with persistent hepatitis B infection.

Hepatic Abscess: mortality 23%; pyogenic liver abscesses cause 0.007-0.03% of hospital admissions in temperate districts but ≈ 0.09% in Thailand

Agents: 50% mixed anaerobes (especially Gram positive cocci; also *Odoribacter splanchnicus*); *Staphylococcus aureus*, coliforms, *Actinomyces*, *Burkholderia pseudomallei, Yersinia pseudotuberculosis, Chromobacterium violaceum* (in 44% of infections), *Listeria monocytogenes* (in diabetes), *Streptococcus milleri*, *Edwardsiella tarda* (rare), *Haemophilus influenzae* (adult), *Haemophilus parainfluenzae*, *Klebsiella pneumoniae* (in diabetics; especially serotype K1), *Entamoeba histolytica* (resulting from hepatic amoebiasis; may rupture into peritoneum, pericardium, pleura or lung), *Schistosoma*, *Toxocara*

Diagnosis: incubation period > 21 d in amoebic; night sweats in 75% of amoebic; liver enlargement in 69-76% of bacterial, 95-100% of amoebic (presenting complaint in 40%); fever in 63-100% of bacterial, 35-95% of amoebic (< 38°C in 60%; presenting complaint in 40%); nausea/vomiting in 60-75% of amoebic; raised right diaphragm in 60% of amoebic; epigastric pain and tenderness in 48-52% of amoebic; right upper quadrant pain and tenderness in 47-69% of bacterial, 66-100% of amoebic (presenting complaint in 30%), 57% of actinomycotic; chills in 42-70% of amoebic; right shoulder pain in 40% of amoebic (presenting complaint in 3%); anorexia/weight loss/fatigue in 33-100% of amoebic (presenting complaint in 5%), 3% of actinomycotic; back pain in 30% of amoebic; diarrhoea in 25-66% of amoebic (50% bloody; presenting complaint in 15%); right chest pain in 6-50% of amoebic; hiccoughs occasionally in amoebic; right pleural effusion in 35% of amoebic; geographic history; epidemiological history; ultrasonography; radioactive isotope scan (positive in 89% of pyogenic; large,

single defect in right lobe in amoebic); arteriogram (positive in 77% of pyogenic); upper gastrointestinal X-ray (positive in 19% of pyogenic; elevated right hemidiaphragm in 60% of amoebic); micro and culture of biopsy, aspirated fluid (in amoebic, trophozoites found only at periphery of cavitary lesions and aspirates may be falsely negative; sensitivity is only 20-30%); serology (amoebic; complement fixation test (evaluated), bentonite flocculation (evaluated), indirect hemagglutination (commercially available; with counterimmunoelectrophoresis, most sensitive (70%) and specific (70-80% in acute, > 90% in convalescent)), latex agglutination (commercially available), indirect immunofluorescence (evaluated), immunodiffusion (agar gel diffusion; commercially available), immunoelectrophoresis, counterimmunoelectrophoresis (commercially available; with indirect haemagglutination, most sensitive and specific), ELISA (commercially available; dot ELISA for antibody as sensitive as indirect hemagglutination and better than plate ELISA and has 100% specificity); animal inoculation (monkey, ferret); trophozoites or cysts in stool (25% of amoebic); white cell count > 10,000/μL in 87% of pyogenic and 62-90% of amoebic (42-60% 10,000-20,000/μL); elevated prothrombin time in 80% of amoebic; anemia in 95% of actinomycotic, 31-70% of amoebic (haemoglobin 10-14 g/dL in 66-70%), also in pyogenic; hematocrit 80-100% of normal in 52% of amoebic, < 35% in 50% of pyogenic; elevated ESR in 95% of actinomycotic; leucocytosis in 93% of actinomycotic; serum albumin decreased in 23-60% of amoebic, 3 g/dL in 33% of pyogenic; serum alkaline phosphatase > 10 IU/mL in 55-60% of pyogenic, increased in 91% of actinomycotic and in 23-60% of amoebic (< 130 IU in 60% of acute cases but > 130 IU in 90% of chronic cases); serum bilirubin 2 mg/dL in 53% of pyogenic, increased in 13-26% of amoebic; serum glutamic-oxaloacetic acid transaminase > 40 U/mL in 51% of pyogenic, < 40 IU in 45-73% of amoebic; serum lactic dehydrogenase normal in 93% of amoebic; globulin elevated in 56% of amoebic

Differential Diagnosis (Amoebic): pyogenic liver abscess, hepatic neoplasm, hydatid cysts; male gender, insidious onset, fever, history of chronic diarrhoea (only in 30-40% of patients), right pleuritic pain, single hepatic lesion of right lobe, liver enlargement, liver tenderness, liver filling defect favour diagnosis

Treatment: aspiration +:

***Chromobacterium violaceum*:** chloramphenicol

***Actinomyces*:** penicillin, tetracycline

Klebsiella pneumoniae: ceftriaxone

Other Bacterial: ciprofloxacin + metronidazole

***Entamoeba histolytica*:** metronidazole 750 mg orally or i.v. 8 hourly (child: 35-50 mg/kg/d in 3 doses) for 10 d or tinidazole 2 g orally daily for 3-5 d or 600 mg twice daily for 10 d (child: 50 mg/kg/d for 3-5 d); emetine 1 mg/kg/d to 60 mg maximum in 2 divided doses for 5 d, followed by chloroquine phosphate 600 mg base orally daily for 2 d, then 300 mg base orally daily for 2-3 w (child: 10 mg base/kg to 300 mg maximum daily for 2-3 w) if no response to metronidazole in 72 h; percutaneous or surgical drainage if no response to chemotherapy after 5 d, abscess > 10 cm, or suspected impending rupture; if concomitant cyst passing detected, presume cysts pathogenic and treat with diloxanide furoate 500 mg 3 times daily (child: 20 mg/kg/d in 3 divided doses) for 10 d or diodohydroxyquine to eliminate carrier state

HEPATIC GRANULOMA

Agents: 20% *Mycobacterium tuberculosis*, 2% *Brucella*, 2% *Schistosoma*, 1% fungi (*Histoplasma capsulatum*, *Cryptococcus neoformans*, *Coccidioides immitis*, *Ajellomyces dermatitidis*, *Candida*, *Torulopsis*, *Aspergillus*), 1% viruses (*human cytomegalovirus*, *Epstein-Barr virus*, *human hepatitis A virus*, *human hepatitis B virus*, *influenzavirus B*); atypical mycobacteria, *Mycobacterium bovis BCG*, *Mycobacterium leprae* (in 90% of lepromatous cases, 20% of tuberculoid), *Francisella tularensis*, *Klebsiella granulomatis, Burkholderia pseudomallei, Listeria monocytogenes, Nocardia, Actinomyces, Salmonella typhi, Salmonella paratyphi B, Coxiella burnetii, Treponema pallidum subsp pallidum, Chlamydia, Toxocara, Fasciola, Capillaria, Strongyloides, Ascaris, Ancyclostoma, Entamoeba histolytica, Toxoplasma, Plasmodium,* Pentastomida; 35% sarcoidosis, 10% cirrhosis, 2% lymphomas, 1% drug-induced and toxic; others

Diagnosis: histology, microscopy and culture of biopsy; serology; counterimmunoelectrophoresis; bromosulphophthalein retention increased in 80% of sarcoidosis, 73% of tuberculous and 56% of fungal; cholesterol abnormal in 33% of tuberculous, 17% of fungal, normal in sarcoidosis; serum alanine aminotransferase decreased in 50% of sarcoidosis, 47% of tuberculous, 25% of fungal; serum bilirubin increased in 37% of tuberculous, 18% of sarcoidosis, normal in fungal; serum gamma globulin increased in 86% of fungal, 83% of sarcoidosis, 68% of tuberculous

Tuberculosis: fever of unknown origin, frequently with chills, anemia, meningeal involvement, loss of weight and asthenia, symptoms < 6-8 mo

Treatment:

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L;

regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Other Mycobacteria: 4-6 of ethionamide, cycloserine, viomycin, ethambutol, pyrazinamide, capreomycin

***Brucella*, *Francisella tularensis*, *Klebsiella granulomatis*:** streptomycin

***Burkholderia pseudomallei*, *Nocardia*, *Toxoplasma*:** cotrimoxazole + ceftazidime or meropenem or imipenem

***Listeria monocytogenes*:** ampicillin

***Salmonella*:** chloramphenicol

***Actinomyces*:** penicillin

Fungi: amphotericin B 0.75 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 14 d

***Entamoeba histolytica*:** metronidazole, emetine + chloroquine

***Schistosoma*:** praziquantel, niridazole, sodium stibogluconate

***Plasmodium*:** chloroquine

Fasciola: bithionol

Capillaria: no known treatment

Pentastomida: levamisole

Other Parasites: thiabendazole

Viral: mainly non-specific

Unknown: isoniazid + steroids

BACILLARY PELIOSIS: blood-filled peliotic changes in hepatic or splenic parenchyma; especially in AIDS

Agents: *Bartonella henselae, Bartonella quintana*

Diagnosis: Warthin-Starry stain of biopsy

Treatment: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 3-4 mo (not < 8 y), erythromycin 10 mg/kg to 500 mg orally 6 hourly for 3-4 mo, erythromycin ethyl succinate 20 mg/kg to 800 mg orally 6 hourly fo 3-4 mo

MALARIAL SPLENOMEGALY: occurs in areas where malaria is endemic

Agent: *Plasmodium* species

Diagnosis:

Hyperreactive Malarial Splenomegaly (Tropical Splenomegaly Syndrome): elevated serum IgM level, high malarial antibody titre, lymphocytic infiltration of hepatic sinusoids; parasitemia rare; decreases with long-term corticosteroid therapy

Nonimmune Malarial Splenomegaly: serum IgM and malarial antibody levels not elevated; occurs in the absence of immunity during acute malarial attacks, recrudescences or epidemics

Treatment:

Hyperreactive: corticosteroids

Nonimmune: antimalarials

SPLENIC ABSCESS

Agents: *Staphylococcus aureus*, *Salmonella*, *Escherichia coli*, *Propionibacterium acnes*, *Propionibacterium avidum*, *Listeria monocytogenes*, *Clostridium difficile*, *Shigella flexneri* (extremely rare), *Streptococcus pneumoniae* (rare), *Streptococcus equinus* (rare), *Mycobacterium tuberculosis* (in AIDS), *Allejomyces dermatitidis* (rare), others

Diagnosis: computed tomography, ultrasonography; culture of biopsy or surgical specimen

Treatment: resection +:

***Staphylococcus aureus*:** cloxacillin

***Salmonella*, *Escherichia coli*:** chloramphenicol

***Propionibacterium*:** penicillin

***Listeria monocytogenes*:** ampicillin

***Clostridium difficile*:** vancomycin, metronidazole

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Streptococci: benzylpenicillin 18 MU/d i.v. + gentamicin 240 mg/d i.v. for 2 w, then amoxycillin 1.5 g/d oral + clindamaycin 900 mg/d oral

***Ajellomyces dermatitidis*:** amphotericin B, ketoconazole

LYMPH GLAND INFECTIONS

Agents: 36% *Mycobacterium* (23% of cervical lymph node infections in children; 20% *Mycobacterium tuberculosis* (5% of tuberculosis cases; 5% of cervical lymph node infections in children), 12% *Mycobacterium avium-intracellulare*, 4% *Mycobacterium kansasii; Mycobacterium scrofulaceum* (frequent cervical in children); infrequent *Mycobacterium chelonae, Mycobacterium fortuitum* (cervical), *Mycobacterium haemophilum, Mycobacterium malmoense*), 35% fungal (27% *Histoplasma capsulatum*, 3% *Ajellomyces dermatitidis*, 2% *Coccidioides immitis*, 2% *Cryptococcus neoformans*, 1% *Sporothrix schenckii,* rare *Aspergillus*), 3% *Staphylococcus aureus* (79% of cervical lymph node infections in children); *Brucella* (in 50% of infections), *Corynebacterium pseudotuberculosis, Listeria monocytogenes, Yersinia pestis* (pea-sized to orange-sized inguinal, axillary), *Francisella tularensis* (painful; neck, axillary, epitrochlear), *Toxoplasma gondii* (localised or general)

Diagnosis: Gram stain, Ziehl-Neelsen stain, fluorescent antibody stain, direct immunofluorescence and culture of lymph node; histology; serology

Cervical: mildly tender, small to moderate nodes usually secondary to viral upper respiratory tract infection; large, tender anterior nodes associated with phyaryngitis/tonsillitis; large tender nodes with skin erythema and fever occur in Kawasaki syndrome, *Epstein-Barr virus* infections and cat scratch disease; acute suppurative secondary to local staphylococcal skin infection, streptococcal tonsillopharyngitis or dental infection; chronic or subacute unilateral usually mycobacterial

Tuberculosis: nodes usually in supraclavicular area or posterior cervical triangle, more commonly bilateral; pulmonary tuberculosis may be present; constitutional symptoms prominent

***Brucella*:** acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Other Bacterial Infections: fever usually present; nodes may be warm and tender; pharyngitis may be present

Toxoplasmosis: IgM-IFA, DS-IgM-ELISA, serial IgG tests; biopsy

Differential Diagnosis: cat scratch disease (usually unilateral and suppurates—similar to nontuberculous mycobacterial infection; history of cat scratch; skin tests), infectious mononucleosis (blood picture, heterophil antibody test, specific tests for *Epstein-Barr virus*), lymphoma (involvement of other sites may be present), leukemia (blood picture, bone marrow examination)

Treatment:

Suppurative: di/flucloxacillin 25 mg/kg to 500 mg orally 6 hourly for 7 d, cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for 7 d

***Brucella*:** doxycycline 100 mg orally twice a day + rifampicin 600 mg orally 4 times a day or streptomycin 1 g i.m. 4 times a day for 45 d, ciprofloxacin 500 mg orally twice a day + rifmapicin 600 mg orally twice a day for 30 d

Staphylococcus aureus: di/flucloxacillin 25 mg/kg to 500 mg orally 6 hourly for 7 d, cephalexin 12.5 mg/g to 500 mg orally 6 hourly for 7 d

***Corynebacterium pseudotuberculosis*:** erythromycin or penicillin + surgical drainage or excision

***Mycobacterium chelonae*, *Mycobacterium fortuitum*:** 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

***Listeria monocytogenes*:** erythromycin 500 mg orally 6 hourly (child: 30 mg/kg daily in 4 divided doses) for 5 d

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Other Mycobacteria: ethionamide, cycloserine, viomycin, ethambutol

***Francisella tularensis*:** streptomycin, tetracycline

Yersinia pestis: streptomycin

Fungi: resection; amphotericin B, miconazole (not *Aspergillus*)

***Toxoplasma gondii*:** cotrimoxazole, sulphadiazine + pyrimethamine, spiramycin

LYMPHADENOPATHY: 0.3% of new episodes of illness in UK

Agents: in addition to the above specific infections, a number of agents cause more or less characteristic lymphadenopathy

Preauricular: acute hemorrhagic conjunctivitis (in 77% of cases), epidemic keratoconjunctivitis (in 85% of cases)

Postauricular: rubella (also suboccipital and postcervical)

Cervical: 38% undiagnosed, 17% benign noninfectious causes, 13% cat scratch disease, 12% malignancy, 9% secondary to tonsillitis, sinusitis, parotitis, mastoiditis, otitis, 3% *Toxoplasma gondii,* 2% *Streptococcus pyogenes,*, 1% *Staphylococcus aureus,* 1% *Mycobacterium tuberculosis,* 1% anaerobes, 1% *Epstein-Barr virus*, 1% *simplexvirus 3*, *mumps virus*, tularemia, Lyme disease, *Haemophilus parainfluenzae, Haemophilus aphrophilus, Streptococcus anginosus, Actinomyces israelii, Corynebacterium diphtheriae*, *human cytomegalovirus* (rare), Kawasaki syndrome (68% of cases have an acute nonsuppurative cervical mass > 1.5 cm diameter)

Axillary: anthrax, *Pseudomonas aeruginosa* whirlpool-associated dermatitis (painful; in 14% of cases), psittacosis (also enlarged red lymphoid follicles on posterior pharyngeal wall)

Inguinal: anthrax, chancroid (in 32% of cases; tender, unilateral or bilateral), gonorrhoea, granuloma inguinale, herpes genitalis, lymphogranuloma venereum, *Yersinia enterocolitica* (bilateral)

Near Primary Site of Infection: Chaga's disease, *Pasteurella multocida,* staphylococci, streptococci

Generalised: *human adenovirus 4* (in 7% of cases), *human adenovirus 16* (in 58% of cases), AIDS (persisting 3+ mo), algal infection, chromobacteriosis (in 11% of cases), cryptosporidiosis (in 14% of cases), Gambian trypanosomiasis, Rhodesian trypanosomiasis (fulminating), leprosy, protozoan infection, Rocky Mountain spotted fever (in 27% of cases; 13% in first 3 d), syphilis (primary and secondary)

Diagnosis: clinical; ultrasound; serology; culture, histology and special staining of needle aspiration or extirpated node; PCR of biopsy for cat scratch disease

Treatment: dependent on agent

Lymphangitis occurs with *Brugia malayi* and *Wuchereria bancrofti* infections. Ascending lymphangitis is also seen (rarely) in tularemia.

Mesenteric Lymphadenitis

Agents: adenovirus (intussusception common), measles (in 15% of hospitalised cases), *Yersinia pseudotuberculosis*, Y*ersinia enterocolitica*, *Mycobacterium tuberculosis*

Diagnosis: viral and bacterial culture of biopsy; serology (monospecific saline agglutination titre ≥ 1:128 in previously healthy individual; rise or fall in titre; indirect immunofluorescent antibody test)

***Yersinia pseudotuberculosis*:** ESR 10-105 mm/h, white cell count 5 500-18 500/μL

Treatment: surgery if indicated

***Yersinia*:** gentamicin, cefotaxime, doxycycline, ciprofloxacin

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Cat Scratch Disease (Benign Inoculation Lymphoreticulosis, Benign Lymphoreticulosis, Benign Reticulosis, Cat Scratch Fever, Debré-Mollaret Syndrome, Felinosis, Foshay-Mollaret Syndrome, Inoculation Adenitis, Lymphoreticulosis Benigna, Morbus Petzetakis, Nonbacterial Regional Lymphadenitis, Petzetakis Disease): usually benign; typical presentation (initial cutaneous lesion at site of inoculation, followed by regional lymphadenitis, which often leads to formation of fistulas through which enlarged suppurating lymph nodes drain) in 88% of cases, inoculation lesion (skin, eye, mucous membrane) in 59%, Parinaud's oculoglandular syndrome in 6%, encephalitis in 2%, severe or chronic systemic disease (including abdominal visceral granulomas) in 2%, erythema nodosum in 0.6%, pneumonitis in 0.2%, breast tumour in 0.2%, thrombocytopenia purpura in 0.1%; also mesenteric adenopathy; fatigue, malaise, weight loss, progressively higher and longer recurring fevers, headache and hepatomegaly in HIV-infected patients; spread through cat flea feces

Agent: *Bartonella henselae*

Diagnosis: adenopathy only in 51%, fever in 31% (71% in AIDS), malaise/fatigue in 28% (36% in AIDS), headache in 13%, anorexia, emesis, weight loss in 13% (36% in AIDS), splenomegaly in 12%, sore throat in 9%, exanthem in 4%, conjunctivitis in 4%, swelling of parotid gland in 2%; severe systemic disease and multiple skin sites in 93% of AIDS patients infected; cat contact with presence of scratch or primary dermal or eye lesion; normal blood cells and differential count; Mantoux tests negative; serology for *Epstein-Barr virus*, *human cytomegalovirus*, *Toxoplasma*, fungal diseases, lymphogranuloma venereum, syphilis, *human immunodeficiency virus*, *simplexvirus*, tularemia, brucellosis and streptococci negative; skin test (cat scratch antigen; positive in 98-99% of cases; not in widespread use because antigen difficult to obtain and not standardised); characteristic histopathologic changes in lymph node or skin lesion; demonstration of small, pleomorphic bacilli in collagen fibres, in abscesses or in granulomas, stained by Warthin-Starry silver impregnation method, Brown-Hopps stain or immunoperoxidase stain; PCR; culture usually unsuccessful

Treatment: spontaneous cure in 2-21 mo in normal patients; often severe in AIDS; azithromycin 10 mg/kg to 500 mg orally first day then 5 mg/kg to 250 mg orally once a day for 4 d; aspiration of abscesses or fluctuant nodes as necessary
Prophylaxis: eradication of cat fleas

***EPSTEIN-BARR VIRUS* DISEASE:** widespread, particularly in young; ≈ 14,000 cases/y (17 deaths/y) in USA; 0.01% of new episodes of illness in UK; transmitted by contact with external secretions (saliva); incubation period 7-14 d; inflammatory reaction in all reticuloendothelial organs
Agent: *Epstein-Barr virus*; *simplexvirus 6* primary infection in adults gives similar condition; *human cytomegalovirus* and *Toxoplasma gondii* give similar symptoms but without pharyngitis or heterophil agglutinins; lymphadenopathy and rash are rare with *human cytomegalovirus*
Diagnosis:

Children < 8 y: glandular fever: fever in 90%, splenomegaly in 60%, > 25% atypical lymphocytes in 55%, lymphadenopathy in 50%, hepatomegaly in 45%, abnormal liver function tests in 45%, lymphocytes > 50% of leucocytes in 40%, exudative pharyngitis in 40%, heterophil antibody in 5%, autoantibodies absent

Older Children, Young Adults, AIDS Cases and Organ Transplant Recipients: monocytic angina: sore throat ± increased lymph glands

Young Adults (15-30 y): infectious mononucleosis: lymphadenopathy in 95%, abnormal liver function tests in 95%, lymphocytes > 50% of leucocytes in 90% (> 35% in all) and atypical lymphocytes in all cases (also present with adenovirus, *human cytomegalovirus*, *simplexvirus*, *mumps virus*, *rubella virus*, toxoplasmosis and viral hepatitis and as drug reaction to hydantoinates, paraaminosalicylic acid, phenylbutazone and sulphonamides) but with > 25% atypical lymphocytes in 45% (> 50% lymphocytes with > 10% atypical mononuclears sensitivity 39%, specificity 97%), continued fever in 85%, serum glutamic-pyruvic acid transaminase increased in 84%, serum glutamic-oxaloacetic acid transaminase increased in 83%, serum alkaline phosphatase increased in 81%, heterophil agglutinin antibody (Paul-Bunnell-Davidsohn test) positive (titre 1:128 after absorption by guinea pig and ox cells) in 80-100%, exudative pharyngitis and sore throat (but without conjunctivitis or rhinitis) in 80%, serum gamma globulin increased in 72%, increased leucocytes but decreased neutrophils in 60-80%, bone marrow granulomas in 50%, serum bilirubin increased in 43%, splenomegaly in 40-55%, serum albumin decreased in 36%, autoantibodies in 25%, platelet count slightly decreased in 25-50%, occult hemolysis in 20-40%, blood urea increased in 15-20%, rash in 10-20%, hepatomegaly in 10%, liver damage common; early antigen antibody > 1:20 (sensitivity 90%, specificity 97%; indicates active infection; appears at 1-4 w, duration 6 mo); indirect fluorescent antibody titre or ELISA for IgG, IgA and IgM (viral capsid antigen antibody > 1:650 sensitivity 40%, specificity 100%; IgG appears rapidly after onset, peaks after 1-2 mo, slowly drops to ≈ 1:320, maintained for life; IgM positive in acutely ill, peaks at 2-3 mo); EA:VCA > 0.031 (sensitivity 100%, specificity 97%); Epstein-Barr nuclear antigen antibody positive 2-52 w after onset, persists for life (Pasteur IgG ELISA kit 90% sensitivity, 95% specificity); (generally, VCA IgG negative, VCA IgM negative, EBNA IgG negative = negative; VCA IgG positive, VCA IgM positive, EBNA negative = recent infection; VCA IgG positive, VCA IgM negative, EBNA IgG positive = past infection); cold agglutinins in 10-50% of cases; mitochondrial cytoplasmic fluorescence may be seen in smooth muscle; serum leucine aminopeptidase inconsistently increased; rheumatoid factor may be present; possible complications include hemolytic anemia, aplastic anemia, thrombocytopenia, neutropenia, disseminated intravascular coagulation, airway obstruction, pneumonia, pleural effusion, myocarditis, pericarditis, aseptic meningitis, meningoencephalitis, encephalitis, transverse myelitis, peripheral neuritis, facial nerve palsy, optic neuritis, Guillain-Barré syndrome, hepatic necrosis, Reye's syndrome, splenic rupture
Treatment: aspirin or paracetamol or nonsteroidal anti-iflammatory drug for pain (narcotic analgesics cotnraindicated); prednisolone 0.5 mg/kg for 1-2 w in patients with severe prostration, significant thrombocytopenia or hemolytic anemia; parenteral dexamethasone 0.5-1 mg/kg to 10 mg daily or hydrocortisone 100 mg 6 hourly in impending airway obstruction; famiclovir in severe cases; antimicrobials, especially ampicillin and amoxycillin, should be avoided unless there is concurrent infection with frank bacterial pathogens; drug reactions, especially skin reactions with ampicillin and amoxycillin (widespread maculopapular reaction), are common in this situation and occur also in other viral infections; if streptococcal pharyngitis is suspected, a 10 d course of penicillin or erythromycin should be given

NASOPHARYNGEAL CARCINOMA: tumour of nasal passages and throat; affects up to 2% of people in Southern China; also in Southeast Asia, northern Africa and among Artic peoples; *Epstein-Barr virus* transforms epithelial cell (? + cocarcinogen in food)

BURKITT'S LYMPHOMA may be due to *Epstein-Barr virus* transforming B lymphocytes (evidence compelling but not conclusive; cofactor (? malaria) may be required

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE: tumour often found in organ transplant patients
Agent: ? *Epstein-Barr virus*

ACUTE INFECTIVE LYMPHOCYTOSIS: occurs in children
Agent: ? enterovirus
Diagnosis: absolute lymphocytosis persisting for 2-3 w, eosinophilia common; associated with abdominal pain, diarrhoea and vomiting

Treatment: none

Chronic Non-specific Infectious Lymphocytosis

Agent: unknown

Diagnosis: moderate leucocytosis with lymphocytosis lasting for months, low normal hemoglobin, normal platelet count and ESR; tests for infectious mononucleosis, *human cytomegalovirus* and toxoplasmosis negative

Treatment: none

Adult T Cell Leukemia

Agent: *human T-lymphotrophic virus 1*

Diagnosis: immunoprecipitation

Treatment: as for other leukemias

***Human immunodeficiency virus* (HIV) Infection/Acquired Immunodeficiency Syndrome (AIDS):** worldwide; global prevalence (HIV infection) ≈ 40 M (> 25 M in Subsaharan Africa; 36% of adult population in Botswana infected; malaria important cofactor); leading cause of death in Africa, causing 25% of deaths in South Africa, and fourth leading cause of death worldwide (≈ 20 M deaths to date); ≈ 600 notified cases (≈ 500 deaths)/y in Australia; 0.1% of ambulatory care visits in USA; *Pan troglodytes* (chimpanzee) probable natural host and reservoir; majority of cases sexually transmitted by anal intercourse (risk 0.06-5% per contact), remainder by vaginal intercourse (risk 0.05-0.2% per contact male to female, 0.03-6% female to male), shared use of needles (risk 0.7% per contact), transplantation, blood transfusion (risk 90% per contact), other exposure to contaminated blood (needle puncture risk 0.3% per contact), deep kissing infected individual with bleeding gums, oral sex (infection from fellatio very rare), congenital (≈ 750,000 HIV infected babies born/y globally; virus destroys T4 lymphocytes, weakening resistance to infection by a wide variety of bacteria, protozoa, fungi and viruses and causing an increased incidence of a number of carcinomas

Agent: *human immunodeficiency virus*

Diagnosis: patient history; fever in 87% of primary infections, skin rash in 50-68%; also night sweats, arthralgia, (40-80%) myalgia (40-80%), malaise, headache (40-80%), nausea (10-40%), vomiting (10-40%), diarrhoea (10-40%), anorexia, pharyngitis, weight loss (10-40% > 5 kg), lymphadenopathy (40-80%), sore throat (40-80%), fatigue (40-80%), retro-orbital pain, depression; on examination, 77% have abnormalities of oral cavity (10-40% ulcers), 73% of skin (10-40% genital ulcers) and 57% of lymph nodes; 74% have thrombocytopenia (< $150X10^6$/mL); also leucopenia, meningitis, neuropathy, encephalopathy; in the absence of a known cause of immunosuppression (high dose or long term systemic corticosteroid therapy or other immunosuppressive/cytotoxic therapy, Hodgkin's disease, non-Hodgkin's lymphoma (other than primary brain lymphoma), lymphocytic leukemia, multiple myeloma, any other cause of lymphoreticular or histiocytic tumour, angioimmunoblastic lymphadenopathy, congenital immune deficiency syndrome or acquired immune deficiency syndrome (such as one involving hypogammaglobulinemia) atypical of *human immunodeficiency virus* infection, any disease that is indicative of a defect in cellular immune function (candidiasis of esophagus, trachea, bronchi or lungs; extrapulmonary cryptococcosis; *human cytomegalovirus* infection of organ other than liver, spleen or lymph node in patient > 1 mo; *simplexvirus* causing mucocutaneous ulcer persisting longer than 1 mo, or bronchitis, pneumonitis or esophagitis for any duration affecting patient > 1 mo; Kaposi's sarcoma or primary lymphoma in the CNS in patient < 60 y; meningitis, encephalitis, pneumonitis due to *Pneumocystis jiroveci*, *Toxoplasma* (patient > 1 mo), *Aspergillus*, *Nocardia*, *Candida*, *Strongyloides*, zygomycetes; lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia affecting a child < 13 y; progressive multifocal leucoencephalopathy; chronic cryptosporidial enterocolitis (diarrhoea persisting > 1 mo); disseminated (site other than or in addition to lungs, skin, cervical or hilar lymph nodes) atypical mycobacteriosis (especially *Mycobacterium avium-intracellulare* complex or *Mycobacterium kansasii*), coccidioidomycosis, histoplasmosis, toxoplasmosis of the brain in > 1 mo, 2 or more bacterial infections (septicemia, pneumonia, meningitis, bone or joint infections) or abscess of internal organ or body cavity other than otitis media or superficial abscesses), or any patient with decreased T helper cells, decreased T helper/T suppressor ratio, increased serum globulins, decreased blastogenesis or anergy should be tested for possible AIDS

Low Risk Individuals With No Known Exposure: ELISA (false positives in multiparous women, those recently immunised against influenza or hepatitis B, those who have had multiple blood transfusions, and those with autoimmune disease, cirrhosis due to alcohol use, malaria, dengue or hepatitis B); confirmed with Western blot or immunofluorescence assay

Low Risk Individuals With Possible Exposure: ELISA + Western blot (frequent indeterminate reactions in absence of infection with some kits); repeated at 3, 6, 9 and 12 mo after possible exposure; p24 antigen capture if possible exposure within 6-12 w of evaluation or if patient has mononucleosis-like syndrome, followed by antibody test 4-6 weeks later

High Risk Individuals: ELISA and Western blot repeated at 6 w intervals; culture of peripheral blood lymphocytes or testing for proviral DNA in lymphocytes if negative

AIDS (as opposed to *human immunodeficiency virus* infection) is diagnosed by laboratory evidence + presence of one or more of following diseases: multiple or recurrent septicemia, pneumonia, meningitis, bone or joint infection, or abscess of internal organ or body cavity (excluding otitis media or superficial mucosal abscesses) caused by *Haemophilus*, *Streptococcus*

or other pyogenic bacteria in children < 13 y; disseminated or extrapulmonary coccidioidomycosis; *human immunodeficiency virus*-related encephalopathy; disseminated or extrapulmonary histoplasmosis; cryptosporidiosis or isosporidiosis with diarrhoea persisting > 1 mo; Kaposi's sarcoma; primary lymphoma of the brain; B cell non-Hodgkin's lymphoma; small noncleaved lymphoma or immunoblastic sarcoma of unknown immunologic phenotype; disseminated or extrapulmonary mycobacterial disease; pulmonary or extrapulmonary disease caused by *Mycobacterium tuberculosis*; recurrent nontyphoidal *Salmonella* septicemia; HIV wasting syndrome; candidiasis of esophagus, bronchi, trachea or lungs; *human cytomegalovirus* retinitis with loss of vision; *human cytomegalovirus* disease other than liver, spleen or nodes; lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia affecting a child < 13 y; *Pneumocystis jiroveci* pneumonia; toxoplasmosis of brain affecting patient > 1 mo; invasive cervical cancer; chronic ulcers (> 1 mo duration), bronchitis, pneumonitis or esophagitis due to *simplexvirus*; recurrent pneumonia; progressive multifocal leucoencephalopathy; in the absence of serological evidence, the diagnosis of AIDS will be accepted if all other indicators listed above are excluded and any of the indicator diseases listed above are present and the T helper/inducer ($CD4^+$) lymphocyte count is < 200/μL; any patient with proven *human immunodeficiency virus infection* and with one or more of the indicator diseases listed above or with $CD4^+$ T cell count < 200/μL is to be considered as meeting the definition of AIDS; cases of *human immunodeficiency virus* infection with $CD4^+$ counts > 200/μL are classified category B if they display any of the following symptoms: bacillary angiomatosis, oropharyngeal candidiasis, vulvovaginal thrush which is persistent or frequent or poorly responsive to therapy, moderate or severe cervical dysplasia/cervical carcinoma in situ, such constitutional symptoms as fever (38.5°C) or diarrhoea lasting > 1 mo, oral hairy leucoplakia, shingles involving at least 2 distinct episodes or > 1 dermatome, idiopathic thrombocytopenic purpura, listeriosis, pelvic inflammatory disease (particularly if complicated by tubo-ovarian abscess), peripheral neuropathy; *human immunodeficiency virus* infections with $CD4^+$ counts < 200/μL and any of the above conditions are grouped as category A

Treatment: may be deferred until patient symptomatic or CD4 cell count < 350/μL; [emtricitabine + tenofovir 200 + 300 mg daily (not child) or lamivudine + zidovudine 150 + 300 mg 12 hourly (not child) or lamivudine 150 mg 12 hourly or 300 mg daily + tenofovir 300 mg daily (not child) or abacivir 300 mg 12 hourly or 600 mg daily + emtricitabine 200 mg daily (not child) or abacivir + lamivudine 600 + 300 mg daily (not child) or didanosine (< 60 kg: 250 mg daily; > 60 kg: 400 mg daily) + emtricitabine 200 mg daily (not child) or didanosine (child: 120 mg/m² (150 mg/m² in neurological disease) 12 hourly; adult < 60 kg: 250 mg daily; > 60 kg: 400 mg daily) + lamivudine (child: 4 mg/kg to 150 mg 12 hourly; adult: 150 mg 12 hourly or 300 mg daily)] + efavirenz (10-15 kg: 200 mg daily; 16-20 kg: 250 mg daily; 20-25 kg: 300 mg daily; 25-32.5 kg: 350 mg daily; 32.5-40 kg: 400 mg daily; > 40 kg: 600 mg daily; not in pregnant or likely to become pregnant) or nevirapine 120 mg/m² to 200 mg daily for 2 w then 12 hourly (not in women with CD4 cell count > 250/μL or men with CD4 cell count > 400/μL) delavirdine 400 mg 8 hourly (not < 12 y) or lopinavir + ritonavir 400 + 100 mg 12 hourly (child ≥ 2 y: 230 + 57.5 mg/m² 12 hourly) or atazanavir 400 mg daily or 300 mg daily + ritonavir 100 mg daily (not child) or fosamprenavir 700 mg + ritonavir 100 mg 12 hourly (not child) or fosampernavir 1400 mg + ritonavir 200 mg daily (treatment naïve only; not child) or indinavir 800 mg 8 hourly (not child) or 800 mg + 100 mg ritonavir 12 hourly (not child) or nelfinavir 25-35 mg/kg to 750 mg 8 hourly or 45-55 mg/kg to 1250 mg 12 hourly or saquinavir 1200 mg 8 hourly (soft gel capsules only; not child) or 1000 mg + ritonavir 100 mg 12 hourly (not child)

Treatment Failure: enfuvirtide 2 mg/kg to 90 mg s.c. 12 hourly (not < 6 y)

Prophylaxis:

Low Risk Exposure: lamivudine + zidovudine 4 + 10 mg/kg to 150 + 300 mg orally 12 hourly for 4 w, emtricitabine + tenofovir 200 + 300 mg orally daily for 4 w

High Risk Exposure: lopinavir + ritonavir 400 + 100 mg orally 12 hourly for 4 w, nelfinavir 25 mg/kg to 1.25 g orally 12 hourly for 4 w

Pregnancy: zidovudine + caesarean section (2% risk of vertical transmission)

HIV WASTING SYNDROME

Agent: *human immunodeficiency virus*

Diagnosis: *human immunodeficiency virus* infection + profound involuntary weight loss of > 10% of baseline body weight + either chronic diarrhoea (at least 2 loose stools/d for ≥ 30 d) or chronic weakness and documented fever (for ≥ 30 days; intermittent or constant) in absence of a concurrent illness or condition other than *human immunodeficiency virus* infection that could explain the findings (eg, cancer, tuberculosis, cryptosporidiosis or other specific enteritis)

Treatment: as for **AIDS** + increased fluids, calories and protein, smoking cessation, regular exercise; recombinant growth hormone for muscle wasting

VIRUS-ASSOCIATED HEMOPHAGOCYTIC SYNDROME: fulminant disorder associated with systemic viral infection

Agents: *Epstein-Barr virus*, *human cytomegalovirus*, adenovirus, *simplexvirus 1* and *2* , *human herpesvirus 6*

Diagnosis: multiple organ infiltration of hemophagocytic histiocytes into lymphoreticular tissues

Treatment: supportive

Chapter 11

Infections of the Skeletal System

JOINT PAIN IN CHILDREN

Single Joint:

Without Constitutional Symptoms: chondromalacia patellae, osteochondritis dissecans, other osteochrondritides, Osgood-Schlatter's disease, Sever's disease, Pertle's disease, slipped femoral epiphysis

Signs of General Disease: leukemia, histiocystosis, sickle cell hemoglobin

With Constitutional Upset: acute infections of joints and bones, juvenile rheumatoid arthritis, Henoch-Schonlein purpura, sickle cell hemoglobin, subacute bacterial endocarditis

Multiple Joints: juvenile rheumatoid arthritis and other connective tissue disorders, multiple septic arthritis or osteomyelitis, rheumatic fever, anterior poliomyelitis, rickets, scurvy, purpura, non-accidental injury

ARTHRITIS

Agents: Reiter syndrome (48% of inflammatory arthritis in young men; oligoarticular and asymmetrical, predominantly lower extremity), ankylosing spondylitis (18% of inflammatory arthritis in young men), rheumatoid arthritis (8% of inflammatory arthritis in young men), psoriatic arthritis (7% of inflammatory arthritis in young men), systemic lupus erythematosus (5% of inflammatory arthritis in young men), acute rheumatic fever (3% of inflammatory arthritis in young men), Behcet's disease (2% of inflammatory arthritis in young men), gouty arthritis (2% of inflammatory arthritis in young men), Henoch-Schonlein purpura (2% of inflammatory arthritis in young men; may be complication of *Epstein-Barr virus* infection), septic arthritis (1% of inflammatory arthritis in young men), Crohn's arthritis (1% of inflammatory arthritis in young men), sarcoid arthritis (1% of inflammatory arthritis in young men), Lyme arthritis (in 52% of cases; 29% knee, 14% shoulder, 12% hip, 11% ankle, 9% wrist, 8% hand, 6% foot, 3% toes), yersinosis (in 11% of *Yersinia enterocolitica* and 55% of *Yersinia pseudotuberculosis* cases), Kawasaki syndrome (in 29% of cases), dermatomyositis (in 25% of cases), acute viral hepatitis (in 15% of cases), scleroderma (localised form; in 10% of cases), brucellosis (arthritis in 9% of cases; arthralgia in 55%), *Ross River virus* (poly, especially knees and wrists), *rubella virus* (transient poly), Mucha-Habermann disease, osteochondrosis (limited to maturing lower skeleton), Sweet's syndrome, Takayasu's arteritis

Diagnosis: erythrocyte sedimentation rate 47 mm/h in ankylosing spondylitis, elevated in all cases of foreign body arthritis, 90% of discitis cases, 80% of cases of Kawasaki syndrome, also in Mucha-Habermann disease, multicentric osteomyelitis (mild to moderate), Sweet's syndrome and Takayasu's arteritis

Synovial Fluid Examination:

Normal: straw-coloured, clear, no fibrin clot, good mucin clot, < 200 leucocytes/μL, $< 25\%$ polymorphs, glucose $\approx 100\%$ blood level

Reiter syndrome: turbid, large fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/μL, $> 50\%$ polymorphs, glucose $\approx 75\%$ blood level

Ankylosing Spondylitis: turbid, large fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/μL, $> 50\%$ polymorphs, glucose $\approx 75\%$ blood level

Rheumatoid Arthritis: clear to turbid, large (2-4+) fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/μL, $> 66\%$ polymorphs, glucose $\approx$ 50-75% blood level

Psoriatic Arthritis: turbid, large fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/μL, $> 50\%$ polymorphs, glucose $\approx 75\%$ blood level

Acute Gout or Pseudogout: turbid, large (2-4+) fibrin clot, fair to poor mucin clot, 5000-50,000 leucocytes/μL, $> 70\%$ polymorphs, glucose $\approx 90\%$ blood level

Rheumatic Fever: slightly turbid, 1-2+ fibrin clot, good mucin clot, 18,000 leucocytes/μL, 50% polymorphs, difference between blood and synovial fluid glucose $= 10$

Tuberculous Arthritis: turbid, large (2-3+) fibrin clot, poor mucin clot, $\approx$ 20,000-25,000 leucocytes/μL, polymorphs variable (usually 60%), glucose $< 50\%$ blood level; acid-fast stain positive in 20%, cultures positive in 80%, biopsy positive in 95%

Other Bacterial Septic Arthritis: very turbid or purulent, large (2-4+) fibrin clot, poor mucin clot, 10,000-100,000 leucocytes/μL, $> 80\%$ polymorphs, glucose $< 50\%$ blood level; Gram stain positive in 50-75%, culture positive

***Candida* Septic Arthritis:** 46,000-56,000 leucocytes/μL, 79-97% polymorphs, glucose 18-113 mg/dL, protein 2.8-3.7X serum

Arthritis Associated With Intestinal Diseases: turbid, large fibrin clot, fair to poor mucin clot, 5,000-50,000 leucocytes/μL, $> 50\%$ polymorphs, glucose $\approx 75\%$ blood level

Degenerative Joint Disease: clear to slightly turbid, small (0-1+) fibrin clot, good mucin clot, ≈ 700-2000 leucocytes/μL, < 25% polymorphs, glucose ≈ 100% blood level

Foreign Body Arthritis: ≈ 60% inflammatory

Traumatic Arthritis: straw-coloured, bloody or xanthochromic, small (0-1+) fibrin clot, good mucin clot, 50-1200 leucocytes/μL, < 25% polymorphs, glucose ≈ 100% blood level, protein 2-3X normal

REACTIVE ARTHRITIS (REITER SYNDROME)

Agents: *Shigella, Salmonella, Yersinia enterocolitica, Yersinia pseudotuberculosis, Campylobacter* (hips and lower back; uncommon), *Vibrio parahaemolyticus, Clostridium difficile, Chlamydia, human immunodeficiency virus*, *Cyclospora,* others

Diagnosis: micro and culture of synovial fluid (very high cell count, glucose 80 mg/dL, culture negative), blood tests (moderate anemia, moderate neutrophilia, ESR raised; Rose-Waaler and latex negative; serology may be positive; specific organisms may be cultured); culture of feces (for enteric organisms listed); culture and immunofluorescence of any urethral discharge; HLA typing

***Shigella*:** typically sets in 10 d after enteritis; days 1-11 urethritis, days 3-7 conjunctivitis, day 4-month or more polyarthritis (may become permanent or recurrent, with erythrocyte sedimentation rate increased in each recrudescence)

***Yersinia*:** in adults, joint symptoms resembling rheumatoid arthritis; in children, polyarthritis and erythema nodosum resembling rheumatic fever; direct agglutination test, indirect immunofluorescence of intestinal biopsy

Treatment: appropriate antimicrobial treatment of any relevant organisms isolated (*Shigella*, *Salmonella*, *Yersinia*: gentamicin, cefotaxime, doxycycline, ciprofloxacin; *Campylobacter*: erythromycin; *Clostridium difficile*: metronidazole, vancomycin; *Chlamydia*: tetracycline, doxycycline, erythromycin); bed rest and aspirin; phenylbutazone + indomethacin

ANKYLOSING SPONDYLITIS: chronic arthritis of spine; immune response to bacterial antigen cross-reacts with joint antigen, giving autoimmune damage; strong association with HLA B27 genotype

Agent: *Klebsiella*

Diagnosis: synovial fluid examination; HLA typing

Treatment: phenylbutazone + indomethacin

RHEUMATIC FEVER: an acute febrile disease occurring as a sequela, nearly always after a latent period of 2 to several weeks, to an untreated or inadequately treated streptococcal respiratory tract disease (especially pharyngitis)

Agent: *Streptococcus pyogenes*

Diagnosis: manifestations and their severity vary widely, but usually (≈ 75% of cases) include polyarthritis with intense migrating arthralgia; there may be no objective features or clinically evident arthritis with heat, redness, swelling and tenderness; knees, ankles, elbows and wrists most affected joints; > 1 joint involved in ≈ 50% of patients; with therapy, average duration of attacks is about 3 mo; carditis occurs in about 1/3 of cases; chorea is not common and erythema marginatum and subcutaneous nodules are now even less so, but these conditions are diagnostically important should they occur

Prophylaxis: benzathine penicillin (≤ 20 kg: 450 mg; > 20 kg: 900 mg) i.m. at 3-4 weekly intervals or phenoxymethylpenicillin 250 mg orally 12 hourly or (if penicillin hypersensitive) erythromycin 250 mg orally 12 hourly or erythromycin ethyl succinate 400 mg orally 12 hourly; continue minimum 5 y (until at least 18 y) if without carditis or evident valve disease, minimum 10 y (until at least 25 years) if mild or moderate carditis or mild residual valve disease, for life if severe carditis or moderate to severe residual valve disease, or before surgery

SEPTIC ARTHRITIS: can be life threatening and frequently associated with significant morbidity

Agents: almost any organism may be introduced directly or hematogenously; *Staphylococcus aureus* (63% of hospital admissions; neonates, children over 2 y, 25% of total adult cases, usually chronic underlying disease, especially diabetes and rheumatoid arthritis; also Stage I and Stage III prosthetic infections; most common cause of chronic infective arthritis; 17% methicillin resistant), 20% streptococci (mainly *Streptococcus pyogenes* (15% of total adult cases; hematogenous spread from respiratory or skin infection; also Stage III prosthetic infections), *Streptococcus agalactiae* (Stage III prosthetic infections), *Streptococcus pneumoniae* (50% primary focus in lung, middle ear; associated meningitis, endocarditis; alcohol abusers; 6% of community acquired infections; mortality 19% in adults, <1% in children; 56% in knee in adults; bacteremia in 72% of adult cases), Group C streptococci), *Enterococcus faecalis* (seventh most common cause of chronic infective arthritis), 10% Gram negative bacilli (chronic debilitating diseases, such as diabetes, malignancy, immunosuppressive drugs; urinary tract infection may precede; neonates; alcoholics; also Stage III prosthetic infections; *Proteus* second and *Klebsiella* fifth most common cause of chronic infective arthritis; *Haemophilus influenzae* (infants 1-18 mo, young children, debilitated adults; preceding meningitis in 30%, osteomyelitis in 22%; 8% of all *Haemophilus influenzae* systemic disease in children), *Haemophilus parainfluenzae, Brucella* (in 9-37% of infections), *Salmonella* (< 20 y; related to sickle cell disease; *Salmonella typhi* (fourth most common cause of chronic infective arthritis), *Salmonella paratyphi C*, *Salmonella choleraesuis*, *Salmonella typhimurium* (in renal transplant recipients), *Capnocytophaga*, *Mycoplasma hominis* (associated with prostheses), *Eikenella corrodens* (in 50% of infections related to human bites or fist fight injuries), *Kingella kingae* (mainly infants and young children; ≈ ½ of cases in knee), *Pseudomonas aeruginosa* (complicating puncture wounds of foot in children; i.v. drug abusers; third most common cause of chronic infective arthritis), *Burkholdeia cepacia*, *Serratia marcescens* (i.v. drug abusers; may involve

sternoclavicular or sacroiliac joint), *Moraxella catarrhalis* (rare), *Ureaplasma urealyticum* (in hypogammaglobulinemia), *Streptobacillus moniliformis* (rare complication of rat-bite fever), *Campylobacter fetus subsp fetus* (uncommon), *Moraxella osloensis* (rare), *Pasteurella multocida* (polyarticular) and *Pasteurella pneumotropica* (dog and cat bite or exposure), *Haemophilus paraprophilus, Legionella pneumophila* (1 case reported in immunosuppressed patient)), 4% *Mycobacterium tuberculosis* (reactivation of latent disease; chronic, insidious, monoarticular; knee most common; most do not have concomitant active pulmonary tuberculosis; PPD almost always positive; differs from Poncet's disease, which is polyarthritis occurring during acute tuberculosis infection but in which no mycobacterial infection can be found), *Neisseria gonorrhoeae* (gonococcal arthritis (blenorrhagic arthritis, gonorrhoeal arthritis); 17% of community acquired infections; 50% of total adult cases; arises as a consequence of disseminated gonococcal disease; previously healthy adult, predominates in young women, often within 1 w of onset of menses or last trimester of pregnancy; initial migratory polyarthritis, synovitis or tenosynovitis (wrist, dorsum of hands or feet, Achilles' tendon), typical skin lesions during septicemic phase of disseminated gonococcal disease or localised arthritis, often with purulent joint fluid, in post-septicemic stage; knee or wrist most common), *Neisseria meningitidis* (2% of meningococcal infections; in 5% of children and 11% of adults with acute meningococccal disease (allergic, hemarthrosis and iatrogenic probably more common than septic); oligoarticular; appears as meningitis is resolving; also in chronic meningococcemia and primary infections), *Staphylococcus epidermidis* (catheter induced in neutropenics; Stage I and Stage III prosthetic infections; sixth most common cause of chronic infective arthritis), *Listeria monocytogenes* (rare), anaerobes (Stage II prosthetic infections), *Arcanobacterium haemolyticum* (posttraumatic), *Corynebacterium xerosis* (following vascular surgery), *Arcanobacterium pyogenes, Corynebacterium diphtheriae*, *Corynebacterium kutscheri, Neisseria mucosa* (rare), *Erysipelothrix rhusiopathiae, Candida* (*Candida albicans* and *Candida tropicalis* 17% of hospital acquired infections; especially in knee in cancer patients; insidious onset, indolent course; may occur in debilitated patient; males > females; usually 40s-50s; also *Candida parapsilosis* and *Candida glabrata* in prostheses), *Scedosporium* (penetrating trauma, surgery)
Diagnosis: mono- or oligoarticular, lower > upper extremity, fever, local inflammation, pain with motion; micro (predominance of polymorphs), culture (mycobacteria and *Legionella* in Bactec 13A medium), counterimmunoelectrophoresis and latex agglutination of synovial fluid; blood cultures; white cell count 18,000-100,000/μL; increased erythrocyte sedimentation rate

***Brucella*:** acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis
Treatment: surgical drainage in all hip joint infections, inadequate closed drainage, persistent febrile course, inaccessible joint; needle drainage in other cases except prosthetic, where resection of prosthesis and all foreign bodies (including cement fragments) and debridement of involved tissues is required (especially in fungal infections)

Organism Not Known:

< 5 y Old: di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly for 3-6 d + cefotaxime 50 mg/kg to 2 g i.v 8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. once daily for 3-6 d, then di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly or (if *Haemophilus influenzae* likely) amoxycillin-clavulanate 15 mg/kg to 500 mg orally 8 hourly for minimum 21 d total

Sexually Active Young Adult: single dose ceftriaxone 125 mg i.m or single dose ciprofloxacin 500 mg orally + doxycycline 100 mg twice a day for 7 d

Adult: flucloxacillin + gentamicin or flucloxacillin + oral ciprofloxacin

With Prosthesis: vancomycin + third generation cephalosporin

***Neisseria*:** benzylpenicillin 150 000 U/kg i.v. daily in divided doses for 7 d, ceftriaxone 50 mg/kg to maximum 3 g i.v. daily for 7 d, cefoxitin 100 mg/kg i.v. daily in divided doses for 7 d, erythromycin 50 mg/kg daily orally in 4 divided doses for 7 d

***Kingella kingae*:** benzylpenicillin 4 MU i.v. at once, then 2 MU i.v. 4 hourly (neonates: 100,000 U/kg daily in 3 or 4 divided doses; < 45 kg: 250,000 U/kg daily in divided doses) for at least 10 d, followed by phenoxymethylpenicillin 1 g orally 6 hourly for 3-7 w (< 12 y: 25-50 mg/kg orally daily in 4 divided doses)

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

***Staphylococcus aureus*:** di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly for 2-4 w, then di(flu)cloxacillin 25 mg/kg to 1 g orally 6 hourly for at least 6 w total ± probenecid 10 mg/kg to maximum 500 mg orally 6 hourly for minimum 6 w total; if methicillin resistant, vancomycin 20 mg/kg to 1 g i.v. slowly 12 hourly for 2-6 w, then rifampicin 7.5 mg/kg to 300 mg orally 12 hourly + sodium fusidate 12 mg/kg to 500 mg orally 12 hourly

Penicillin Hypersensitive: cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 25 mg/kg to 1 g i.v. or i.m. 8 hourly, then cephalexin 25 mg/kg to 1 g orally 6 hourly; if severe, clindamycin 10 mg/kg to 450 mg i.v. slowly 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly, then clindamycin 300-450 mg orally 6-8 hourly (child: 10 mg/kg to 450 mg orally 6 hourly)

Streptococci, *Capnocytophaga*, *Arcanobacterium haemolyticum*, *Streptobacillus moniliformis*: benzylpenicillin 100 000-150 000 U/kg/d i.v. for 10-14 d (4 w for *Streptococcus pneumoniae*)

***Brucella*:** streptomycin 1 g twice a day i.m. for 14-21 d + rifampicin 900 mg/d orally for 45 d + doxycycline 100 mg orally twice daily for 45 d

***Haemophilus influenzae*, *Eikenella corrodens*:** cefotaxime 2 g i.v. 4 hourly (child: 200 mg/kg daily in 4 divided doses) or ceftriaxone i.v. for 4-6 days, then amoxycillin-clavulanate for total period of 21 d; chloramphenicol

***Listeria monocytogenes*:** ampicillin 2 g i.v. 8 hourly for 10 d, then amoxycillin 500 mg orally 3 times daily

***Salmonella*:** joint aspiration, surgical drainage; chloramphenicol 500 mg orally 6 hourly (child > 2 w: 50 mg/kg orally daily in 4 divided doses; premature, newborn and those with immature metabolism: 25 mg/kg daily in 4 divided doses) for 15 d

Coliforms, *Pseudomonas aeruginosa*, *Serratia marcescens*: gentamicin or tobramycin 5 mg/kg/d i.v. for 4-6 w (+ ticarcillin in immunocompromised host with *Pseudomonas aeruginosa*)

***Burkholderia cepacia*:** imipenem

***Corynebacterium*:** i.v. cefotaxime 2 g 3 times daily for 21 d, followed by oral erythromycin 500 mg 4 times daily for 14 w

***Campylobacter fetus* subsp *fetus*:** gentamicin, erythromycin, amoxycillin-clavulanate

***Mycoplasma hominis*:** ciprofloxacin 750 mg twice daily, tetracycline, doxycycline

***Ureaplasma urealyticum*:** tetracycline, doxycycline

***Candida tropicalis, Candida glabrata*:** amphotericin B

Other *Candida*: oral ketoconazole + i.v. miconazole, amphotericin B

***Scedosporium*:** debridement

Test of Progress: complement fixation

VIRAL ARTHRITIS

Agents: *Ross River virus*, *Barmah Forest virus*, *hepatitis A virus*, hepatitis B virus (in 10-42% of cases; usually preicteric), *hepatitis C virus*, *mumps virus* (polyarticular or monoarticular; mainly adult males; self-limited), infectious mononucleosis (in 5-10% of cases), *human cytomegalovirus*, *simplexvirus 1*, *human echovirus*, *simplexvirus 3*, adenovirus (in 8% of *human adenovirus E* serotype 4 infections), group A arboviruses (rash, encephalitis, nephritis and hemorrhage), *human rubella virus* (usually adult women; fingers, wrists and knees; also vaccine), *human parvovirus B19*

Diagnosis: arthralgias common; usually transient; fever; leucocytosis with neutrophilia, raised erythrocyte sedimentation rate, mild anemia; agglutinations (paired sera 2 w apart)

***Human parvovirus B19*:** PCR on synovial fluid or joint aspirate, dot hybridisation, capture ELISA (IgG) on serum

Treatment: corticosteroids, non-steroidal anti-inflammatory drugs (not aspirin)

ARTHRALGIA also occurs in 77% of dengue cases (poly), 73% of acute schistosomiasis attacks, 73% of cases of Mediterranean spotted fever, 56% of influenza A cases, 50% of cases of Rocky Mountain spotted fever, 35% of *human immunodeficiency virus* infections, 25% of loiasis, in infections with *Bacillus anthracis*, *Coxiella burnetii*, *Francisella tularensis*, *Listeria monocytogenes*, *Pasteurella multocida* and *Streptobacillus moniliformis*, in malaria, Marburg virus disease, plague, psittacosis (generalised) and Rift Valley fever; also in arthromyalgia, leukemia (severe) and pigmented villonodular synovitis (+ swelling; knee, hip, ankle, tarsus, elbow)

OSTEOMYELITIS AND OSTEOCHONDRITIS: secondary to an adjacent infection (overlying abscesses or burns, but usually from decubitus ulcers in patients without generalised vascular insufficiency and due to *Staphylococcus*, Gram negative bacilli (especially *Pseudomonas aeruginosa*) and anaerobes; in patients with generalised vascular insufficiency, such as with diabetes or peripheral vascular disease, the small bones of the feet are most commonly infected with *Staphylococcus*, *Enterococcus*, Gram negative bacilli and anaerobes), while necrotising/malignant otitis externa (usually due to *Pseudomonas*) also occurs; osteomyelitis of the fingers is a common complication of fingertip abscess); hematogenous (femur or tibia involved in most childhood cases; vertebrae next most common—45% lumbar, 35% thoracic, 10% cervical, 10% thoracicolumbar, 10% lumbosacral, 20% due to *Staphylococcus*, 15% Gram negative rod, 3% *Streptococcus*, 30% from a genitourinary infection, 5% from skin, 5% from respiratory, less acute in adults and surgery is usually not necessary but 10% suffer paraplegia and 5% die; long bone infection is commonly a reactivation and due to *Staphylococcus*,

Peptostreptococcus, *Pseudomonas aeruginosa*); due to penetrating wounds (animal bites, iatrogenic heel puncture in children, other puncture wounds of the foot; *Pseudomonas* most common); due to compound fracture; due to infection of prosthesis; postoperative (postoperative pubic osteomyelitis may be misdiagnosed as osteitis pubis); multifocal (typical in neonates and drug addicts); 30% femur, 25% tibia, 15% vertebra, 10% humerus, 5% pelvis, 5% fibula, 5% tarsal, 2% radius, 2% rib

Agents: 55% *Staphylococcus aureus* (60% in children; 30% of neonatal; most common cause of osteomyelitis secondary to contiguous focus), 22% *Staphylococcus aureus* + anaerobes, 5% anaerobes alone (*Bacteroides fragilis*, *Peptostreptococcus*, *Propionibacterium*, *Actinomyces,* rare *Veillonella parvula*), 5% *Streptococcus pyogenes*, 3% *Pseudomonas aeruginosa* (66% in drug abusers; spine, sacroiliac joint, sternoclavicular joint, symphysis pubis, as well as usual large joints, in these patients; second most common cause of osteomyelitis secondary to contiguous focus), 2% *Streptococcus pneumoniae* (< 1% in children), 1% *Mycobacterium tuberculosis* (lower thoracic, proximal femur, distal femur, proximal tibia, ankle); *Streptococcus canis* (sacroiliitis), *Streptococcus agalactiae* (40% of neonatal), other β-hemolytic streptococci (including Group C), *Streptococcus viridans*, enterococci, *Streptococcus milleri*, *Streptococcus equinus* (rare spondylodiskitis and vertebral osteomyelitis as complication of endocarditis), coagulase negative staphylococci, *Escherichia coli*, *Klebsiella*, *Enterobacter, Proteus, Serratia* (spine, sacroiliac joint, sternoclavicular joint, symphysis pubis as well as usual large joints, in drug addicts), *Mycobacterium fortuitum* (emerging pathogen in AIDS), *Haemophilus influenzae* (3% of non-bacteremic invasive *Haemophilus influenzae* infections in older children and adults), *Brucella*, *Salmonella* (associated with hemoglobinopathies, particularly sickle cell disease; more likely in patients with lymphoma or connective tissue disorders), *Neisseria meningitidis*, *Neisseria sicca* (following back injury), *Aeromonas* (post-traumatic), *Clostridium botulinum* (in wound botulism), *Listeria monocytogenes*, *Capnocytophaga*, *Eikenella corrodens* (in 50% of *Eikenella corrodens* infections related to human bites or fist fight injuries), *Nocardia asteroides*, *Haemophilus aprophilus* (rare vertebral), *Haemophilus parainfluenzae* (vertebral), *Kingella kingae* (mainly infants and young children), *Actinobacillus actinomycetemcomitans* (uncommon), *Vibrio vulnificus* (trauma in seawater), *Burkholderia cepacia* (cervical), *Moraxella osloensis* (rare), *Acinetobacter calcoaceticus*, *Ochrobacterium antropi* (puncture wound), *Providencia*, *Plesiomonas shigelloides*, *Pasteurella multocida* and *Pasteurella pneumotropica* (dog and cat bite or exposure), *Haemophilus haemoglobinophilus, Haemophilus paraprophilus, Mycobacterium intracellulare, Mycobacterium simiae* (infrequent), mixed aerobes and anaerobes (skull or facial bones secondary to ENT procedures; long bone compound fractures; pelvic bone secondary to intraabdominal sepsis; hand secondary to bites, especially human; foot associated with vascular insufficiency and/or diabetes; cervical spine secondary to retropharyngeal abscess), *Bartonella henselae* (vertebral), *Candida* (especially in drug abusers, also periprosthetic; vertebral in lengthy treatment with broad spectrum antibiotics, major surgery, hyperalimentation, neutropenia, sternal in coronary artery bypass grafting), *Aspergillus* (predisposing factors, liver transplantation), *Drechslera* (associated with prior surgery), *Scedosporium* (penetrating trauma, surgery), *Cryptococcus neoformans*

Diagnosis: X-ray (82% of cases of vertebral osteomyelitis show intervertebral disc space narrowing); micro and culture of aspirate, swab or biopsy; blood cultures; counterimmunoelectrophoresis of serum; erythrocyte sedimentation rate usually elevated; white cell count (acute: 7400 – 73,000/μL (mean 21,100/μL); chronic traumatic: 8300 – 12,700/μL (mean 9800/μL); chronic prosthetic: 8300/μL); fluorodeoxyglucose-positron emission tomography 96% accurate for hip prothesis, 81% for knee prosthesis, 91% for other osteomyelitis

Neonatal: 40% multiple bone involvement (never with *Streptococcus agalactiae*); increasing incidence of *Escherichia coli*; often secondary to complications during pregnancy or delivery (preeclampsia, premature rupture of membranes, etc); also iatrogenic—heel or scalp resulting from infected heel-stick or phlebitis; septic arthritis in 70% of staphylococcal and 35% of *Streptococcus agalactiae* cases; fever in 66% of total cases, 40% of staphylococcal infections, never in *Streptococcus agalactiae* cases; white cell count > 210,000/μL in 40% of staphylococcal and 10% of *Streptococcus agalactiae* infections; swelling in 75% of patients, decreased movement in 55%, erythema in 30%, tenderness in 15%

Children: bone pain, limp or disuse in all, fever in 85%, joint pain in 66%, history of injury in 45%; 30% femur (60% proximal, 30% distal, 10% middle), 30% tibia (50% distal, 45% proximal, 5% middle), 10% pelvis, 10% humerus, 10% fibula, 3% radius; 20% complicating septic arthritis, 20% growth disturbance, 15% restricted motion, 15% deformity, 15% draining sinus, 10% recurrence, 5% chronicity, 5% pathologic fracture, 1% death

Aspergillus: 1,3-β-D-glucan levels increased

Differential Diagnosis: cellulitis, bone infarction, subperiosteal hematoma, traumatic periostitis, bone cyst, eosinophilic granuloma, osteitis deformans, neurofibromatosis, monoarticular rheumatoid arthritis, osteodystrophy in patient on long term dialysis, recurrent multifocal osteomyelitis with pustularis palmoplantaris (very rare, apparently noninfectious), multiple myeloma, primary or metastatic malignancy, congenital syphilis, pyomyositis, wound infection, soft tissue abscess, acute rheumatic fever, septic arthritis

Treatment: debridement of necrotic bone and loculated purulence, reestablishment of vascularity, grafting bony defects, removal of prostheses; surgery if development of neurological abnormalities in vertebral or cranial osteomyelitis or if spread to hip joint in child; nonsteroidal antiinflammatory drugs +:

General Empirical: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly; cephazolin 50 mg/kg to 2 g i.v. 8 hourly

Immediate Penicillin Hypersensitive: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

Acute Neonatal: gentamicin 5-7.5 mg/kg i.v. daily in 2 or 3 divided doses + cloxacillin/flucloxacillin 200 mg/kg daily i.v. in 3 divided doses for 14 d ± fusidic acid 20 mg/kg 12 hourly by i.v. infusion over 2 h for 14 d, followed by cloxacillin/flucloxacillin orally for 6 mo

Gram Negative Infection Suspected, Child < 5 y Not Immunised Against *Haemophilus influenzae* type b: cefotaxime 50 mg/kg to 2 g i.v. 8 hourly; ceftriaxone 50 mg/kg to 2 g i.v. daily + di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly

Diabetic Foot or Contiguous Ulcer: debridement or surgery, biomechanical offloading of mechanical impediments to wound healing; ciprofloxacin or clindamycin or piperacillin-tazobactam or ampicillin-sulbactam + aminoglycoside for 4-6 w; rifampicin 600 mg twice daily + ofloxacin 200 mg 3 times daily for 6 mo

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

***Mycobacterium fortuitum*, *Nocardia asteroides*:** 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

Streptococci: benzylpenicillin 4 MU i.v. once then 2 MU i.v. 4 hourly (child: 150 000-250 000 U/kg daily in 4 divided doses), followed by phenoxymethylpenicillin 1 g orally 6 hourly for 3-7 w (< 12 y: 25-50 mg/kg orally daily in 4 divided doses); drainage at operation and removal of any prosthesis

Methicillin Susceptible *Staphylococcus aureus*: di/flucloxacillin 50 mg/kg to 2 g i.v. 6 hourly, then di/flucloxacillin 25 mg/kg to 1 g orally 6 hourly

Penicillin Hypersensitive (Not Immediate): cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephalozin 50 mg/kg to 2 g i.v. 8 hourly, then cephalexin 25 mg/kg to 1 g orally 6 hourly

Immediate Penicillin Hypersensitive:

Macrolide Susceptible: clindamyicn 10 mg/kg to 450 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly, then clindamycin 10 mg/kg to 450 mg orally 8 hourly

Macrolide Resistant: vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly), then cotrimoxazole 8/40 mg/kg to 320/1600 mg orally 12 hourly or doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not in child < 8 y)

Methicillin Resistant *Staphylococcus aureus:* vancomycin 25 mg/kg to 1 g (child < 12 y: 30 mg/kg to 1 g) i.v. 12 hourly by slow infusion (monitor blood levels and adjust dose accordingly, then rifampicin 7.5 mg/kg to 300 mg orally 12 hourly + sodium fusidate tablets 12 mg/kg to 500 mg orally 12 hourly or fusidic acid 18 mg/kg to 750 mg orally 2 hourly or clindamycin 10 mg/kg to 450 mg orally 8 hourly or cotrimoxazole 8/40 mg/kg to 320/1600 mg orally 12 hourly

***Listeria monocytogenes*, *Eikenella corrodens*:** ampicillin

***Kingella kingae*:** benzylpenicillin 4 MU i.v. once, then 2 MU i.v. 4 hourly (neonate: 100 000 U/kg daily in 3 or 4 doses; < 45 kg: 250 000 U/kg daily in 6 divided doses) for at least 10 d, followed by phenoxymethylpenicillin 1 g orally 6 hourly for 3-7 w (< 12 y: 25-50 mg/kg orally daily in 4 divided doses)

***Brucella*:** streptomycin 1 g twice a day i.m. for 14-21 d + rifampicin 900 mg/d orally for 45 d + doxycycline 100 mg orally twice daily for 45 d

***Burkholderia cepacia*:** imipenem

***Pseudomonas*:** ofloxacin 200 mg/kg orally 3 times daily for 2-4 w (not child), i.v. tobramycin for 7 d

***Vibrio vulnificus*:** doxycycline 100 mg orally or i.v. twice daily + ceftazidime 2 g i.v. 3 times a day or ciprofloxacin 400 mg twice a day for 3 d or gentamicin

***Aeromonas*:** gentamicin

Anaerobes: chloramphenicol, clindamycin

Other Bacteria: ceftriaxone

Fungi: amphotericin B ± flucytosine, itraconazole, fluconazole (all ineffective for *Scedosporium*); debridement with immediate bone grafting desirable if appropriate

Prophylaxis Before Joint Surgery: cloxacillin/flucloxacillin 500 mg i.v. or i.m. immediately specimens taken during surgery + amoxycillin 500 mg i.v. or i.m. at same time and 6 hourly for 48 h + gentamicin on polymethylmethacrylate beads put into joint and left in situ ≈ 19 d

GRANULOMATOUS SYNOVITIS

Agents: *Mycobacterium tuberculosis*, *Mycobacterium kansasii*, *Mycobacterium marinum, Mycobacterium gordonae, Mycobacterium avium, Mycobacterium chelonae*

Diagnosis: Ziehl-Neelsen stain, culture and histology of surgical specimen

Treatment: surgery +:

Mycobacterium avium: ethambutol 15 mg/kg (not < 6 y) orally daily + clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly or azithromycin 10 mg/kg to 500 mg orally daily + rifampicin 10 mg/kg to 600 mg orally daily or rifabutin 5 mg/kg to 300 mg orally daily till culture negative 12 mo

***Mycobacterium chelonae*:** 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole for 6-12 mo

Mycobacterium kansasii: isoniazid 10 mg/kg to 300 mg orally daily [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally daily + ethambutol 15 mg/kg (not < 6 y) orally daily for 18 mo and 12 months negative cultures

Mycobacterium marinum: clarithromycin 12.5 mg/kg to 500 mg orally 12 hourly, cotrimoxazole 4/20 mg/kg to 160/800 mg orally 12 hourly, doxycycline 2.5 mg/kg to 100 mg orally (not < 8 y) 12 hourly for 3-4 mo

Others: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

TENOSYNOVITIS

Agent: *Mycobacterium nonchromogenicum* (chronic of knee)

Diagnosis: culture of biopsy

Treatment: ethambutol, sulphonamides, cotrimoxazole, erythromycin, streptomycin + surgical debridement

BURSITIS

Agents: *Staphylococcus aureus*, coagulase negative staphylococci, β-haemolytic streptococci, *Mycobacterium marinum, Mycobacterium kansasii, Mycobacterium szulgai, Brucella abortus, Haemophilus influenzae, Serratia marcescens, Pseudomonas fluorescens, Enterobacter cloacae, Escherichia coli, Prototheca* (olecranon)

Diagnosis: culture of aspirate

Treatment: repeated aspiration + appropriate antimicrobials; surgical drainage if necessary

CARPAL TUNNEL SYNDROME

Agents: 21% *Mycobacterium tuberculosis*, 19% *Mycobacterium* other than *Mycobacterium tuberculosis,* 14% rubella vaccine, 11% *Borrelia burgdorferi*, 11% rubella virus, 5% *Histoplasma capsulatum*, 5% *Sporothrix schenckii*, 3% *Neisseria gonorrhoeae*, 3% toxic shock syndrome, 1% *Staphylococcus aureus*, 2% β-haemolytic streptococci, 0.8% coagulase negative staphylococci, 0.8% *Enterococcus faecalis*, 0.8% *Clostridium histolyticum*, 0.8% guinea worm

Diagnosis: smear and culture of biopsy

Treatment: surgery + appropriate antimicrobial

COMPOUND FRACTURES

Agents: *Staphylococcus aureus*, Gram negative bacilli, *Clostridium perfringens*

Diagnosis: if infection is evident before treatment or develops despite treatment, Gram stain and culture of tissue or swab

Treatment: treatment should be prophylactic; di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly, or cephalothin 50 mg/kg to 2 g i.v. 6 hourly or cephazolin 25 mg/kg to 1 g i.v. 8 hourly if penicillin hypersensitive (not immediate), or clindamycin 10 mg/kg to 450 mg i.v. 8 hourly or lincomycin 15 mg/kg to 600 mg 8 hourly if immediate penicillin hypersensitvity for 1-3 d + (if wound soiling or tissue damage severe and/or devitalised tissue present) piperacillin + tazobactam 100 + 12.5 mg/kg to 4 + 0.5 g i.v. 8 hourly or ticarcillin + clavulanate 50 + 1.7 mg/kg to 3 + 0.1 g i.v. 6 hourly then amoxycillin + clavulanate 22.5 + 3.2 mg/kg to 875 + 125 mg orally 12 hourly or (penicillin hypersensitive) gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult 4-6 mg/kg) i.v. as single daily dose (adjust dose for renal function) or ciprofloxacin 10 mg/kg to 400 mg i.v. or 15 mg/kg to 750 mg orally 12 hourly + clindamycin 10 mg/kg to 450 mg i.v. or orally 8 hourly or lincomycin 15 mg/kg to 600 mg i.v. 8 hourly then clindamycin 10 mg/kg to 450 mg orally 8 hourly; review patient's immune status to tetanus

PAGET'S DISEASE: localised deformation of bone

Agent: ? *measles virus* persistent infection of osteoclasts

Chapter 12

Eye Infections

EYE INFECTIONS: A large number of local and systemic conditions of non-infectious origin are reflected in the eye and may mimic eye infections. However, the most common cause of failure to isolate organisms from an apparent infection is prior use of local antimicrobial preparations.

PURULENT CONJUNCTIVITIS: 2% of new episodes of illness in UK; 0.5% of ambulatory care visits in USA

Agents: *Haemophilus* (mainly nontypeable *Haemophilus influenzae* (especially young children; 62% of cases bilateral; conjunctival injection in 86% of cases, purulent discharge in 77%), also *Haemophilus aegyptius*), *Streptococcus pneumoniae* (occasional ophthalmia neonatorum, outbreaks in students and military recruits, sporadic), *Streptococcus pyogenes*, other streptococci (α, β, microaerophilic), *Staphylococcus aureus* (ophthalmia neonatorum), *Moraxella lacunata* (Axenfeld conjunctivitis (diplobacillary conjunctivitis, Morax-Axenfeld conjunctivitis, subacute conjunctivitis); not significant cause in certain areas), *Moraxella catarrhalis*, *Escherichia coli*, *Neisseria gonorrhoeae* (gonococcal conjunctivitis (gonococcal ophthalmia, gonorrhoeal conjunctivitis, gonorrhoeal ophthalmia); acute purulent conjunctivitis usually unilateral in adults (blennorrhoea adultorum) and bilateral in newborn infants (blennorrhoea neonatorum); may lead to corneal ulceration and, if untreated, to impairment or loss of vision), *Neisseria meningitidis* (rare except in central and northern Australia; corneal ulcers in 16%; systemic disease in 18%, with 13% case-fatality rate in those cases), *Neisseria mucosa* (rare neonatal), *Acinetobacter calcoaceticus, Corynebacterium diphtheriae* (uncommon; resulting from inoculation into eye), *Mycobacterium tuberculosis, Corynebacterium striatum* (rare), *Vibrio parahaemolyticus*, *Vibrio alginolyticus, Capnocytophaga*, *Pseudomonas aeruginosa* (antecedent corneal trauma, contact lens wear, concurrent serious systemic disease), *Stenotrophomonas maltophilia* (occasional), *Kingella indologenes* (rare), *Listeria monocytogenes*, *Erysipelothrix rhusiopathiae*, *Bacillus subtilis*, *Candida* (*Candida albicans* common; *Candida tropicalis, Candida stellatoidea, Candida parapsilosis, Candida glabrata* infrequent to rare); any organism other than a light growth of coagulase negative staphylococcus, *Corynebacterium* species other than *Corynebacterium diphtheriae* or *Corynebacterium striatum*, or *Streptococcus viridans*, should be considered possibly significant

Diagnosis: moderate injection, moderate to profuse exudate, follicles absent, no preauricular node enlargement; *Moraxella lacunata* mainly affects area of the canthi; Gram stain and culture of swab of pus or conjunctiva

Gonococcal in Neonate: age 2-4 d at onset, bilateral, marked edema, copious purulent discharge; polymorphs and Gram negative diplococci in smear

Treatment:

***Neisseria meningitidis*:** ceftriaxone 25 mg/kg to 1 g i.m. daily for 3-5 d

Neisseria gonorrheae:

Neonates:

Penicillinase Negative: benzylpenicillin 15 mg/kg i.v. 12 hourly during first week of life and 7.5 mg/kg thereafter for total of 7 d

Penicillin Resistant or Susceptibility Not Known: cefotaxime 50 mg/kg i.v. 8 hourly for 7 d or ceftriaxone 50 mg/kg i.v. daily for 7 d

Others: procaine penicillin 50 mg/kg to 1.5 g i.m. daily for 1-3 d, amoxycillin 75 mg/kg to 3g + probenecid 25 mg/kg to 1 g (not < 2 y) orally daily for 1-3 d

Penicillinase-Producing, Penicillin Hypersensitive: ceftriaxone 25 mg/kg to 1 g i.m. or i.v. as single dose or cefotaxime 25 mg/kg to 1 g i.m. or i.v. as single dose

Mycobacterium tuberculosis requires specialised attention; corticosteroids must not be used

***Staphylococcus aureus* (Serious Ophthalmia Neonatorum):** i.v. cloxacillin for 7 d

***Listeria monocytogenes*:** ampicillin 2 g i.v. 4 hourly (< 1 w: 100 mg/kg daily in 2 divided doses; 1-4 w: 200 mg/kg daily in 3 divided doses; older children: 200-400 mg/kg daily in 4 divided doses) for 2 w + gentamicin 1.3 mg/kg (child: 1.5-2.5 mg/kg) 8 hourly; benzylpenicillin 15-20 MU (neonates: 500 000-1 MU; older children: 200,000-400,000 U/kg) daily in divided doses for 2 w + gentamicin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly; cotrimoxazole 320/1600 mg (child: 8/40 mg/kg) i.v. daily in divided doses

Pseudomonas aeruginosa: topical tobramycin $\pm$ parenteral aminoglycoside $\pm$ ticarcillin or piperacillin

Stenotrophomonas maltophilia: cotrimoxazole $\pm$ rifampicin

***Haemophilus aegyptius* (BPF Clone):** oral rifampicin 20 mg/kg/d for 4 d

Other Bacteria:

Mild: propamidine isethionate 0.1% 1-2 drops 3-4 times daily for 5-7 d

More Severe: chloramphenicol 0.5% eye drops topically 1-2 drops every 2 h, decreasing to 4 times daily as infection improves + chloramphenicol 1% eye ointment topically at night for 3-5 d or framycetin 0.5% eye drops 1-2 drops every 1-2 h, decreasing to 8 hourly as infection improves

***Candida*:** amphotericin B + flucytosine

Prophylaxis:

***Neisseria gonorrhoeae* in Neonates:** single application of 0.5% erythromycin ointment, 1% tetracycline ointment or 1% silver nitrate

Neisseria meningitidis: ceftriaxone 250 mg (child 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children)

Chlamydial Conjunctivitis (Endemic Paratrachoma, Inclusion Blennorrhoea, Inclusion Conjunctivitis, Occidental Paratrachoma, Oculogenital Inclusion Conjunctivitis, Paratrachoma): transmitted to eye from infected genital secretions, also via secretions and fomites in endemic areas; acute or chronic, with conjunctival follicles and mucopurulent discharge

Agent: *Chlamydia trachomatis*

Diagnosis:

Neonatal (Inclusion Conjunctivitis of Newborn, Ophthalmia Neonatorum): age 7-10 d at onset, unilateral or bilateral, redness and moderate edema of lids, copious purulent or mucopurulent discharge, diffuse conjunctival injection; culture, cytology (polymorphs and intracytoplasmic inclusions on Giemsa stain) and immunofluorescence of scrapings from conjunctiva

Older Patients: acute or chronic; conjunctival follicles and mucopurulent discharge; culture, cytology and immunofluorescence of scrapings from lower fornix

Treatment:

Adults, Children > 6 kg: azithromycin 20 mg/kg to 1 g orally as single dose to clinical case, care-givers and close children

Children ≤ 6 kg: erythromycin base 10 mg/kg or erythromycin ethyl succinate 20 mg/kg orally 6 hourly for 21 d

Prophylaxis: 0.5% erythromycin ophthalmic ointment, 1% tetracycline ophthalmic ointment

Trachoma (Arlt Disease, Arlt Trachoma, Egyptian Ophthalmia, Military Ophthalmia): affects 15% of world's population; very common in developing countries, especially N Africa and Arab countries; in Australia, mainly in Aborigines; ≈ 10 cases/y in USA; usually chronic immunopathologic disease in which more severe progressive trachoma infections (active trachoma characterised by follicle formation and papillary hypertrophy in conjunctiva, vascularisation and corneal infiltration (pannus), followed by healed trachoma in which there is scarring of eyelids and cornea, sometimes leading to partial or total loss of sight) occur only after reinfection; transmission by contact with infectious discharge

Agent: *Chlamydia trachomatis*

Diagnosis: follicle formation and papillary hypertrophy in conjunctiva, infiltration of cornea, scarring of lids and cornea; cytology (Giemsa stain sensitivity 29%, specificity 100%) and immunofluorescence (Microtrak-methanol fix sensitivity 78%, specificity 100%), culture (sensitivity 76%, specificity 100%), DNA probe (sensitivity 84%, specificity 96%) of scrapings from upper tarsus; serology

Treatment: as for **Chlamydial Conjunctivitis**

Prophylaxis (5-14 y): oily tetracycline drops, 1 drop once daily for 5 consecutive days in each school month

Prevention and Control: hygiene; treatment of cases; fly control

Nonpurulent Conjunctivitis ('Pink Eye'): common in children

Agents: *simplexvirus 1*(uncommon; may involve cornea; occasional ophthalmia neonatorum), *simplexvirus 3*, *measles virus* (46% of hospitalised measles cases also develop bacterial conjunctivitis), *human rubella virus*, dengue, sandfly fever, *human echovirus 17* and *18*, *coxsackievirus A9*, *Newcastle disease virus*, adenovirus (common cause of swimming pool conjunctivitis; *human adenovirus C* serotypes 1, 2, 5, 6, *human adenovirus B* serotypes 3, 7, *human adenovirus E* serotype 4, *human adenovirus D* serotypes 8, 9, 10, 17, 19, 37, *human adenovirus B* serotype 16 (in 50% of infections)), *human enterovirus 70*, *influenza A virus*, *influenza B virus* (eye discharge and discomfort in 8% of cases), *human cytomegalovirus* in AIDS, Rocky Mountain spotted fever (in 30% of cases; 13% in first 3 d), Crimean-Congo hemorrhagic fever, Mediterranean spotted fever (in 32% of cases), infectious mononucleosis, *Chlamydia*, *Acanthamoeba, Acinetobacter* (contact lenses); also toxic shock syndrome, allergic, caused by silver nitrate prophylaxis, caused by unshielded mercury vapour lamps, sensitivity reaction, chemical irritants

Diagnosis: intact vision, mild pain, mild diffuse injection, minimal exudate present, photophobia absent, lacrimation and pupil normal, follicles present, preauricular node enlargement; cytology, immunofluorescence and viral culture of swab of mucus or corneal or conjunctival scraping; serology

***Acanthamoeba*:** Giemsa-Wright, Wheatley trichrome, calcfluor white/methylene blue, fluorescein conjugated lectin, Gomori methenamine silver, PAS or immunofluoresecent stain and culture of scraping from corneal ulcer; electron microscopy of biopsy

Treatment:

***Chlamydia*:** erythromycin

Acinetobacter:

Mild: propamidine isethionate 0.1% 1-2 drops 6-8 hourly for 5-7 days

More Severe: (polymyxyin B sulphate 5000 U/mL + chloramphenicol 0.5% or neomycin 2.5 mg/mL) 1-2 drops hourly, decreasing to 6 hourly as infection improves + eye ointment as above at bedtime for 3-5 d; chloramphenicol 0.5% eye drops topically 1-2 drops at least 4 times daily to both eyes for 3-5 d + chloramphenicol 1% eye ointment topically at night for 3-5 d; chloramphenicol eye ointment topically 6 hourly for 3-5 d; oily tetracycline eye drops 1-2 drops at least 4 times daily to both eyes for 3-5 d

Acanthamoeba: propamidine isethionate, dibromopropamidine isethionate, clotrimazole + neomycin or gentamicin, Baquacil (10^3 dilution)

***Human herpesvirus 1*:**

Mild: aciclovir 3% eye ointment 1 cm 3 hourly, idoxuridine 0.1% eye drops 1 drop in each eye every h during day and every 2 h at night till improvement, idoxuridine 0.5% eye ointment 1 cm 4 times daily and at night, vidarabine 3% eye ointment 1.5 cm 5 times daily at 3 hourly intervals, reducing to twice daily for 7 d after reepithelialisation has occurred

Severe: aciclovir 5 mg/kg (< 12 y: 250 mg/m^2) 8 hourly i.v. as 1 h infusion for 5 d

***Human herpesvirus 3*:** cool compresses, topical lubrication, topical broad spectrum antibiotic

Allergy: sodium cromoglycate drops

Others: cold compresses, artificial tears, phenylephrine 0.12%, avoidance of bright light, systemic analgesics

ACUTE HEMORRHAGIC CONJUNCTIVITIS: highly contagious; due to poor hygiene

Agents: *human adenovirus B* serotype 11, *human coxsackievirus A24*, *human enterovirus 70*; conjunctival hemorrhages and injection also occur in 57% of cases of hemorrhagic fever with renal syndrome

Diagnosis: conjunctival congestion, bilateral conjunctival injection and irritation in 93% of cases, conjunctival watering, scanty white to profuse watery discharge; viral culture of conjunctival swab; hemagglutination inhibition test

Treatment: betamethasone drops

CONJUNCTIVAL CONGESTION AND INJECTION also occur in 88% of cases of Kawasaki syndrome

CONJUNCTIVAL HYPEREMIA is present in 80% of toxic shock syndrome cases

CONJUNCTIVAL SUFFUSION is common in psittacosis

CONJUNCTIVITIS AND KERATITIS (KERATOCONJUNCTIVITIS)

Agents: *human adenovirus D* serotypes 7, 8, 19, 37, *human adenovirus A* serotype 18 (in developed countries, epidemic and primarily iatrogenic and affecting mainly adults; in developing countries, endemic and primarily disease of children), *simplexvirus 1*, *simplexvirus 3*, AIDS, *Listeria monocytogenes*, *Acinetobacter* (contact lens), *Acanthamoeba* (contact lens)

Diagnosis: eye redness in 98% of cases, eye discharge in 95%; fluorescein staining of cornea; culture of nasopharyngeal swab, swab or scraping of conjunctiva and cornea, feces; cytology, immunofluorescence and culture of corneal or conjunctival scraping; serology

***Acanthamoeba*:** Giemsa-Wright, Wheatley trichrome, calcfluor white/methylene blue, fluorescein conjugated lectin, Gomori methenamine silver, PAS or immunofluoresecent stain and culture of scraping from corneal ulcer; electron microscopy of biopsy

Treatment:

Adenovirus: non-specific

***Simplexvirus 1*:** aciclovir 3% ophthalmic ointment 5 times daily for 14 days or for at least 3 d after healing + atropine 1% 1 drop 12 hourly for duration of treatment

***Simplexvirus 3*:** famciclovir 250 mg orally 8 hourly for 7 d (500 mg orally 8 hourly for 10 d in immunocompromised), valaciclovir 1 g orally 8 hourly for 7 d, aciclovir 20 mg/kg to 800 mg orally 5 times daily for 7 d (preferred in children and in pregnancy); if sight is threatened, aciclovir 10 mg/kg i.v. 8 hourly, each infusion administered over a period of 1 h, for 7 days (adjust dose for renal function); aciclovir 3% eye ointment 5 times daily may be added

Epithelial Keratitis: debridement or none

Stromal Keratitis: topical steroids

Neurotropic Keratitis: topical lubrication, topical antibiotics for secondary infections, tissue adhesives and protective contact lenses to prevent corneal perforation

***Listeria monocytogenes*:** ampicillin or benzylpenicillin + gentamicin, cotrimoxazole

Acinetobacter: topical tobramycin, polymyxyin B

KERATITIS AND IRITIS: 0.01% of new episodes of illness in UK

Agents: *simplexvirus 1*, *simplexvirus 3*, *human immunodeficiency virus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Moraxella lacunata*, α-haemolytic streptococci, Gram negative bacilli (associated with soft contact lenses), *Mycobacterium chelonae, Mycobacterium fortuitum* (emerging pathogen in AIDS), *Mycobacterium tuberculosis, Aspergillus*, *Fusarium, Curvularia, Drechslera, Alternaria; Acinetobacter, Acanthamoeba castellanii, Acanthamoeba culbertsoni, Acanthamoeba hatcheti, Acanthamoeba polyphaga* and *Acanthamoeba rhysoides* (associated with soft contact lenses, hot tubs, unsterile water); also interstitial keratitis due to congenital syphilis or complication of tuberculosis or leprosy, *Sarcopodium oculorum*

Diagnosis: vision may be compromised, severe pain, injection localised to iris ('ciliary flush'), exudate absent, photophobia present, lacrimation increased, pupil contracted; cytology and culture of swabs, scrapings of cornea, corneal biopsy; immunodiffusion, immunofluorescence

***Acanthamoeba*:** Giemsa-Wright, Wheatley trichrome, calcfluor white/methylene blue, fluorescein conjugated lectin, Gomori methenamine silver, PAS or immunofluoresecent stain and culture of scraping from corneal ulcer; electron microscopy of biopsy

Treatment:

***Simplexvirus 1, simplexvirus 3*:** see **CONJUNCTIVITIS AND KERATITIS**

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Other *Mycobacterium*: sulphacetamide drops

Other Gram Positive Bacteria: povidone iodine ± topical prednisolone

Gram Negative Bacilli: topical tobramycin, polymyxyin B

Fungi: topical pimafucin ± ketoconazole; keratoplasty

***Acanthamoeba*:** propamidine isethionate, dibromopropamidine isethionate, clotrimazole + neomycin or gentamicin, Baquacil (10^3 dilution)

PENETRATING EYE INJURIES

Treatment: specialised management required; urgent advice from ophthalmologist mandatory; if significant delay before specialised treatment, vancomycin 20 mg/kg to 1 g i.v. slowly single dose + ciprofloxacin 15 mg/kg to 750 mg orally single dose; gentamicin 5 mg/kg single dose + cefotaxime 50 mg/kg to 1 g i.v. single dose or ceftriaxone 50 mg/kg to 1 g i.v. single dose

ONCHOCERCIASIS (RIVER BLINDNESS): Sub-Saharan Africa, Latin America; incidence 18 M/y; no deaths reported but 270,000 reported cases of blindness annually; transmitted by blackflies, *Simulium*

Agent: *Onchocerca volvulus*; recent report that real culprit is *Wolbachia* carried by the worms

Diagnosis: sclerosing keratitis, chronic iridocyclitis, chorioretinitis, optic atrophy; biopsy of nodule will disclose adult worm, while skin shavings may show microfilariae; slit-lamp eye examination (punctate keratitis, microfilariae in cornea); nodules can be detected by ultrasound; a patch test in which blot of 10% diethylcarbamazine in anhydrous lanolin fixed to skin produces pruritus, edema and papule formation within 72 h is positive in up to 92% of cases; eosinophilia

Treatment: ivermectin 20 µg/kg orally once as a single dose, diethylcarbamazine under expert supervision, suramin (if ocular microfilariae present after diethylcarbamazine and nodulectomy) 50 mg test dose i.v. then 10-15 mg/kg to maximum dose 1 g orally for 5 w, flubendazole 750 mg i.m. once a week for 5 doses; tetracycline to kill *Wolbachia*?

CHRONIC EYE INFECTIONS

Agents: *Pseudomonas*, *Proteus*, *Escherichia coli*, *Klebsiella*, anaerobes, fungi (*Fusarium, Alternaria, Pseudallescheria boydii, Candida albicans,* others)

Diagnosis: culture of corneal, conjunctival scrapings

Treatment: dependent on findings

IRIDOCYCLITIS (CYCLITIS + IRITIS)

Agents: *human herpesvirus 3*, *human immunodeficiency virus*, *Bacillus, Pseudomonas aeruginosa*

Diagnosis: cytology, Gram stain and culture of swabs, scrapings

Treatment:

***Human herpesvirus 3*:** as for **CONJUNCTIVITIS AND KERATITIS**

***Bacillus*:** clindamycin

***Pseudomonas aeruginosa*:** topical tobramycin, polymyxin B

ANTERIOR UVEITIS (CHOROIDITIS + IRIDOCYCLITIS)

Agents: *simplexvirus 1*, *mumps virus*, *simplexvirus 3*, *measles virus*, *human immunodeficiency virus*, *Mycobacterium tuberculosis*, *Treponema pallidum subsp pallidum* (secondary syphilis), *Neisseria gonorrhoeae*, *Brucella*, Rocky Mountain spotted fever, *Leptospira*, *Listeria monocytogenes, Histoplasma capsulatum*, *Toxoplasma gondii*, *Toxocara canis*, *Acanthamoeba*; also rheumatoid arthritis, sarcoidosis, Reiter syndrome, Behcet's disease, inflammatory bowel disease

Diagnosis: smear and culture of aspirate; serology

Treatment: prompt referral to ophthalmologist

***Human herpesvirus 1*, *Human herpesvirus 3*:** see **CONJUNCTIVITIS AND KERATITIS**

***Mycobacterium tuberculosis*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Syphilis: aqueous crystalline penicillin G 3-4 MU i.v. every 4 h or 18-24 MU/d as continuous infusion for 10-14 d, procaine penicillin 2.4 MU i.m. once daily + probenecid 500 mg orally 4 times a day for 10-14 d

***Histoplasma capsulatum*:** amphotericin B, flucytosine, ketoconazole ± steroids

***Toxoplasma*:** corticosteroids + sulphadiazine 1-1.5 g orally or i.v. 6 hourly for 3-6 w then 500 mg orally 6 hourly or 1 g orally 12 hourly + pyrimethamine 50-100 mg orally loading dose then 25-50 mg daily for 3-6 w (continue if necessary)

Sulphadiazine Hypersensitive: substitute clindamycin 600 mg orally or i.v. 6 hourly for 3-6 w

***Toxocara canis*:** thiabendazole

***Acanthamoeba*:** propamidine isethionate, dibromopropamidine isethionate, clotrimazole + neomycin or gentamicin, Baquacil (10^3 dilution)

CHORIORETINITIS (CHOROIDITIS + RETINITIS)

Agents: *Mycobacterium tuberculosis*, *Nocardia*, *Candida*, *Aspergillus*, *Cryptococcus neoformans* (associated with meningitis), *Histoplasma capsulatum*, also sarcoidosis

Diagnosis: clinical; serology; culture of anterior chamber and vitreous aspirates

Treatment:

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Nocardia: cotrimoxazole

Fungi: amphotericin B + steroids

RETINOCHOROIDITIS (RETINITIS + CHOROIDITIS)

Agents: *human cytomegalovirus* (in renal transplantation, AIDS), *simplexvirus 1*, *simplexvirus 3*, *Toxoplasma gondii* (20% of cases of posterior uveitis0, *Toxocara canis*

Diagnosis: clinical; serology; culture of anterior chamber and vitreous aspirates

***Human cytomegalovirus*:** characteristic appearance on serial ophthalmoscopic examinations (eg., discrete patches of retinal whitening with distinct borders, spreading in a centrifugal manner along the paths of blood vessels, progressing over several months, and frequently associated with retinal vasculitis, hemorrhage and necrosis); resolution of active disease leaves retinal scarring and atrophy with retinal pigment epithelial mottling

Toxoplasma: intense white focal area of retinal necrosis with substantial inflammation

***Simplexvirus 3* :** rapid spread; 67% completely blind within 1 mo

Treatment:

***Simplexvirus 1*:** famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

***Simplexvirus 3*:** as for **CONJUNCTIVITIS AND KERATITIS**

***Human cytomegalovirus*:** valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir

5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria ≤ 2+ and creatinine clearance ≥ 55 mL/min) then as above every 2 w

Other Viral: reduction of immunosuppressive therapy

***Toxoplasma*:** pyrimethamine 25 mg 3 times first day then orally daily for 4 w (child: 2 mg/kg to 25 mg maximum daily for 3 d, then 1 mg/kg daily (infant: every second or third d) for 4 w + trisulphapyrimidine or sulphadiazine 2 g then 1 g (child: 50 mg/kg) orally 4 times daily for 4 w + folinic acid 3-9 mg orally daily; clindamycin 300 mg orally 6 hourly (child: 16 mg/kg daily in 3 or 4 doses) for 3-4 w then 150 mg 4 times daily (child: 8 mg/kg daily in 3 or 4 doses) for 3-4 w; spiramycin 1 g twice daily (recommended in pregnancy); azithromycin 500 mg loading dose then 250 mg daily; atovaquone; + corticosteroids; surgery as needed for complications

***Toxocara canis*:** thiabendazole

ENDOPHTHALMITIS: surgery, trauma, penetrating corneal ulcer, systemic infection

Agents: *Staphylococcus aureus* (postoperative, posttraumatic, septicemia), coagulase negative staphylococci (postoperative, posttraumatic), *Propionibacterium acnes* (postoperative), *Corynebacterium* (postoperative), *Streptococcus pneumoniae* (septicemia), *Streptococcus viridans* (conjunctival filtering-bleb associated, bloodborne), *Streptococcus pyogenes* (septicemia, posttraumatic), *Listeria monocytogenes* (oculoglandular listeriosis (angioso-septic listeriosis); uncommon; caused by accidental inoculation into eye), *Bacillus cereus* (posttraumatic, bloodborne), aerobic Gram negative bacilli (< 20% of cases; especially *Proteus mirabilis, Klebsiella pneumoniae* (especially in diabetics), *Escherichia coli* (bloodborne), *Enterobacter* and *Pseudomonas aeruginosa* (postoperative, antecedent corneal ulcers, penetrating trauma, metastatic seeding from bacteremia), *Burkholderia cepacia*, *Aeromonas* (foreign body trauma), *Actinobacillus actinomycetemcomitans* and *Haemophilus paraprophilus* (in association with endocarditis), *Pasteurella multocida* and *Neisseria sp* R-24681 (cat scratch), *Moraxella* (postoperative), *Achromobacter* (postoperative), *Flavobacterium meningosepticum* (postoperative), *Haemophilus influenzae* (postoperative and conjunctival filtering-bleb associated), *Butyrivibrio fibrisolvens* (single case following penetrating injury), *Nocardia asteroides*, *Mycobacterium tuberculosis, Actinomyces* (postoperative), *Candida albicans* and other *Candida* species (associated with parenteral hyperalimentation and in immunocompromised, postoperative, i.v. drug abuse), *Aspergillus* (rare; bloodborne), *Cryptococcus neoformans* (rare; bloodborne), *Scedosporium* and *Pseudallescheria boydii* (in immunocompromised), *Coccidioides immitis* (bloodborne), *Sporothrix schenckii* (bloodborne), *Ajellomyces dermatitidis* (bloodborne), *Histoplasma capsulatum* (bloodborne), other fungi (i.v. narcotic abuse)

Diagnosis: intense pain, decreased visual acuity, marked corneal swelling, lid edema, intense hyperemia of globe, conjunctival chemosis, hypopyon, anterior uveitis, opacity of cornea and vitreous, occasional rupture of globe; Gram stain and Giemsa, methenamine silver or PAS stain, culture (including in blood culture bottle) of aspirate of anterior chamber or vitreous cavity or fine needle retinal biopsy; blood cultures; culture of wound abscess, fistula, conjunctiva

Treatment: vitrectomy or vitreous aspiration if loculated infection or necrotic tissue +:

Empirical Where Delay In Diagnosis: ciprofloxacin 15 mg/kg to 750 mg orally as a single dose + vancomycin 25 mg/kg to 1.5 g (child < 12 y: 30 mg/kg to 1.5 g i.v. as single dose by slow infusion; gentamicin 5 mg/kg i.v. as single dose + cefotaxime 50 mg/kg to 2 g i.v. as single dose or ceftriaxone 50 mg/kg to 2 g i.v. as single dose

***Nocardia*:** cotrimoxazole 20/100 mg/kg/d i.v. for 5 d, then 320/1600 mg orally 4 times a day

Pseudomonas aeruginosa: parenteral, topical, subconjunctival and intraocular antipseudomonal antibiotics

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

Other Bacteria: guided by culture and susceptibility

***Pseudallescheria boydii, Scedosporium*:** azole

Other Fungi:

Severe: intravitreal amphotericin B + dexamethasone

Less Severe: i.v. fluconazole (not *Aspergillus*) or itraconazole

PANOPHTHALMITIS

Agents: *Bacillus cereus* (in drug abusers), *Pseudomonas aeruginosa, Vibrio parahaemolyticus, Mycobacterium tuberculosis*

Diagnosis: Gram stain and culture of tissue aspirate, Ziehl-Neelsen stain and culture of tissue

Treatment:

***Bacillus cereus*:** clindamycin

***Pseudomonas aeruginosa, Vibrio parahaemolyticus*:** gentamicin or neomycin topically and injected beneath Tenon's capsule

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo)

PARASITIC EYE INFECTIONS

Agents: *Taenia solium, Gnathostoma spinigerum, Gnathostoma hispidum, Angiostrongylus cantonesis, Loa Loa* (in 5% of infections), *Multiceps* (cysts usually beneath conjunctiva), *Thelazia callipaeda, Baylisascaris* (from raccoons)

Diagnosis: direct visualisation

Taenia solium: pain on ocular movement, afferent pupillary defect, optic disc edema; combined vector ultrasonography and magnetic resonance imaging; serum ELISA

Multiceps: poor vision and pain in eye

Thelazia: lacrimation, severe pain, scarring, opacities of conjunctiva; may be nervous symptoms and paralysis of ocular muscles

Treatment

Taenia solium: dexamethasone sodium phosphate 100 mg i.v. daily then oral steroids

Others: surgical removal

BLEPHARITIS: 0.3% of new episodes of illness in UK

Agents: commonly seborrhoeic; also viruses (including *simplexvirus 3*), *Staphylococcus aureus*, coagulase negative staphylococci, Gram negative bacilli, fungi, *Demodex brevis*, *Demodex folliculorum*, *Pediculus humanus, Phthirus pubis*

Diagnosis: culture of swab from lid margin, microscopy of epilated eyelashes collected into oil

Demodex folliculorum: usually mild pruritus and fibrous tissue response; rarely, dry chronic erythema with burning irritation and scaling of epidermis

Treatment:

Seborrhoeic: removal of scales from lid margins with 'baby' shampoo or sodium bicarbonate solution; selenium sulphide shampoo of scalp

Simplexvirus 3: cool compresses, topical lubrication, broad spectrum antibiotic

Demodex: occlusive ophthalmic ointment to eyelids and eyelashes

Staphylococcus aureus: as for **Seborrhoeic** + tetracycline hydrochloride 1% ointment, chloramphenicol 1% ointment, or framycetin 0.5% ointment to lid margins once or twice daily until clinically resolved

Associated with Lid Abscess: flucloxacillin 500 mg orally 6 hourly

Other Bacterial: chloramphenicol 1% + polymyxyin B sulphate 5000 U/g ointment to lid margins 3-6 hourly or tetracycline HCl 1% ointment to lid margins 3-6 hourly

Associated with Rosacea: doxycycline 100 mg orally 12 hourly for 2 w, then 100 mg orally daily for 1-2 mo

STYE (EXTERNAL HORDEOLUM): 0.3% of new episodes of illness in UK

Agent: *Staphylococcus aureus*

Diagnosis: pus culture

Treatment: warm compresses, removal of the involved eyelash

MEIBOMIANITIS (INTERNAL HORDEOLUM)

Agents: *Staphylococcus aureus*

Treatment: warm compresses; surgical incision and curettage when necessary; di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly for at least 5 d

Penicillin Hypersensitive: cephalexin 12.5 mg/kg to 500 mg orally 6 hourly for at least 5 d

DACROCYSTITIS, ADENITIS AND CANALICULITIS: 0.04% of new episodes of illness in UK; usually infants or adults > 40 y; unilateral, secondary to blockage of nasolacrimal duct

Agents:

Acute: viruses, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Chlamydia*, *Propionibacterium propionicum* (particularly older males), *Actinomyces*

Chronic: many different bacteria and fungi (especially *Candida albicans*)

Diagnosis: culture and immunofluorescence of canalicular material, conjunctiva

Treatment:

Mild: relief of obstruction, warm compresses; zinc sulphate 0.25% + phenylephrine HCl 0.12% 2 drops 4-8 hourly, with massaging over tear sac before and after instilling drops

Acute and More Severe: di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly

Penicillin Hypersensitive: cephalexin 12.5 mg/kg to 500 mg orally 6 hourly

PRESEPTAL (PERIORBITAL) AND POSTSEPTAL (ORBITAL) CELLULITIS

Agents: *Haemophilus influenzae* (< 5 y of age; following URTI; previously usually type b, now more commonly non-type b; preseptal and postseptal), *Staphylococcus aureus* (postseptal), *Streptococcus pyogenes* (secondary to puncture wounds or lacerations), *Streptococcus pneumoniae* (preseptal and postseptal), aerobic Gram negative bacilli (postseptal), anaerobes (due to trauma, especially human or animal bites; also dental procedures; postseptal), *Pseudomonas aeruginosa, Mucor* and *Aspergillus* (postseptal; immunosuppressed; sinusitis spreading to orbit)

Diagnosis: cultures of swabs of conjunctivae and nearby skin lesions, sinus drainage, abscess drainage or biopsy; blood cultures; sinus and orbital X-rays; CT scanning and ultrasound; lumbar puncture to exclude meningitis

Preseptal: pain, redness, edema of eyelid, low grade fever, inflamed and purulent conjunctiva

Postseptal: fever, headache, swelling of globe, proptosis, marked chemosis, pain on eye movement and compromised eye movement

Treatment:

Bacterial:

Preseptal:

< 5 y:

Child Well: amoxycillin/clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for 7 d or cehpalexin 12.5 mg/kg to 500 mg orally 6 hourly for 7 d

Severely Ill Child: cefotaxime 50 mg/kg to 2 g i.v. 8 hourly or ceftriaxone 50 mg/kg to 2 g i.v. once daily or cefuroxime or ampicillin-sulbactam until response, then amoxycillin-clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for total duration of 7 d; if stye, dacrocystitis, impetigo or wound present, add di/flucloxacillin as below

> 5 y: di(flu)cloxacillin 12.5 mg/kg to 500 mg orally 6 hourly for 7 d or 50 mg/kg to 2 g i.v. 6 hourly for at least 14 d if severe

Postseptal: drainage of abscesses/sinuses; di(flu)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly + ceftriaxone 50 mg/kg to 2 g i.v. once daily or cefotaxime 50 mg/kg to 2 g i.v. 8 hourly, then amxycillin/clavulanate 22.5/3.2 mg/kg to 875/125 mg orally 12 hourly for further 10 d; + 2 antipseudomonal antibiotics in neutropenics

Fungi: amphotericin B + flucytosine

OCULAR MYIASIS (OPHTHALMOMYIASIS, OPHTHALMOMYIASIS EXTERNA, OPHTHALMOMYIASIS INTERNA ANTERIOR, OPHTHALMOMYIASIS INTERNA POSTERIOR): infestation of eye or surrounding tissues by larvae of certain flies

Agents: *Cochliomyia hominivorax, Cochliomyia macellaria*, *Chrysomya bezziana, Chrysomya megacephala, Gasterophilus intestinalis, Hypoderma bovis, Hypoderma lineatum, Oestrus ovis, Rhinoestrus, Wohlfahrtia*

Diagnosis: usually painful conjunctivitis but larvae may also penetrate cornea or reach into tissues of eye, producing serious damage; direct visualisation

Treatment: removal or destruction of larvae if alive; appropriate management of any sequelae

Chapter 13

Thyroiditis

THYROIDITIS

Agents: *Mycobacterium tuberculosis*, *Mycobacterium intracellulare*, *Mycobacterium chelonae, Staphylococcus aureus,* other *Staphylococcus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, other streptococci, Enterobacteriaceae, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Actinobacillus actinomycetemcomitans*, anaerobes, *Aspergillus fumigatus, Aspergillus flavus, Coccidioides immitis, Candida, Pseudallescheria boydii, Echinococcus, Taenia solium*

Diagnosis: histology and culture of biopsy or surgical specimen

Treatment:

***Mycobacterium*:** isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo) ± drainage

Other Bacteria: drainage + antimicrobial agents depending on organism

Fungi: incision or excision + amphotericin B (not *Pseudallescheria boydii*) or flucytosine

Parasites: excision

Chapter 14

Multi-System, Generalised and Disseminated Infections

ADENOVIRUS INFECTIONS: acute respiratory disease (bronchitis, croup, febrile catarrh, rhinitis, sinusitis, laryngotracheitis, tracheobronchitis, pertussis-like syndrome in children < 36 mo, 'influenza-like illness', pharyngitis/sore throat, acute exudative tonsillitis, acute laryngitis, pneumonia, pneumonitis, otitis media, pharyngoconjunctival fever), acute diarrhoea and/or vomiting, intussusception in children, pancreatitis, acute hemorrhagic cystitis in immunosuppressed, non-pyogenic meningitis and meningoencephalitis, maculopapular rash, roseola-like illness, rhabdomyolysis, carditis, myocarditis and pericarditis, mesenteric lymphadenitis, hepatitis, arthritis, follicular conjunctivitis, keratoconjunctivitis, acute hemorrhagic conjunctivitis; disseminated with hepatic necrosis in AIDS, severe combined immunodeficiency, other immunodeficiency; important pathogen in adult bone marrow transplant patients (respiratory infection, urinary tract infection, disseminated disease with hepatitis or conjunctivitis); transmission by droplets, contact; incubation period 2-10 d
Diagnosis: complement fixation test, hemagglutination inhibition antibody technique, neutralisation antibody titre; mild increase in white cell count in 60% of cases; virus isolation in tissue culture from throat and/or conjunctival swabs or pharyngeal washing, feces, CSF (lung tissue post mortem)
Treatment: i.v. ribavirin
Prophylaxis: live, attenuated oral vaccine (experimental)
CYTOMEGALIC INCLUSION DISEASE: worldwide; occurs in noncompromised older children and adults as mononucleosis syndrome (fever, malaise, sore throat, headache, increased levels on liver function tests, atypical lymphocytosis, antibiotic rash common; exudative pharyngitis, splenomegaly, cervical lymphadenopathy, nonspecific rash, anemia less common; icteric hepatitis rare; antinuclear antibodies, rheumatoid factor, cold agglutinins) and in immunocompromised patients (AIDS and after suppressive therapy preceding organ transplantation and after treatment with chemotherapy, steroids or other immunosuppressive agents in other conditions) and as bloodborne disease; encephalitis, myelitis, peripheral neuropathy, polyradiculopathy, chorioretinitis, Guillain-Barré syndrome, intestinal ulceration, pancreatitis, myocarditis, pneumonia, thrombocytopenia purpura, gastrointestinal bleed (particularly in bone marrow transplant recipients 1-3 mo post transplantation); transmission respiratory, blood transfusions (especially cardiac surgery and neonates who require several units of blood); incubation period 1-3 mo
Agent: *human cytomegalovirus*
Diagnosis: fever, leucopoenia, hepatomegaly, splenomegaly, arthralgia; 'glandular fever type atypical mononuclears' in peripheral blood smear; culture of 5 mL of first morning's sample of urine (most dependable source), heparinised blood during acute phase, throat swabs (may be successful weeks or months after acute illness has subsided) using human diploid cell culture; serology by complement fixation test, IgM indirect fluorescent antibody titre test, ELISA (IgG, IgM and IgM capture)

Nonimmunocompromised: IgG seroconversion, presence of IgM antibody specific for *human cytomegalovirus*, urine culture (may reflect remote infection), blood culture

Immunocompromised: demonstration of viral antigen or DNA/RNA in diseased tissue (lung, esophagus, colon), IgG seroconversion (rarely occurs)

Kidney and Liver Transplant Recipients: viral culture by shell vial procedure

Treatment: valganciclovir 900 mg orally 12 hourly for 14-21 d then 900 mg orally daily, ganciclovir 5 mg/kg i.v. twice a day for 2-3 w then 10 mg/kg i.v. 3 times a week or 5 mg/kg i.v. 5 times a week during continued immunosuppression, foscarnet 90 mg/kg i.v. 12 hourly for 2-3 w then 90-120 mg/kg i.v. 5 times weekly, cidofovir 5 mg/kg i.v. weekly for 2 w (+ probenecid if proteinuria $\leq$ 2+ and creatinine clearance $\geq$ 55 mL/min) then as above every 2 w
Prophylaxis

Hematopoietic Stem Cell Transplantation: use of blood products from seronegative donors; ganciclovir 5 mg/kg i.v. every 12 h for 5-7 d, then 5-6 mg/kg i.v. daily for 5 d/w from engraftment until day 100

***Human cytomegalovirus* Seropositive HIV Patient with CD4 Cell Count < 50/µL:** valganciclovir 900 mg orally daily

***REOVIRUS* INFECTIONS:** epidemic viral diarrhoea, non-pyogenic meningitis, acute respiratory illness (pharyngitis, rhinitis), neonatal hepatitis, maculopapular rash
Diagnosis: tissue culture and inoculation of suckling mouse with material from feces and throat swab
Treatment: non-specific
***HUMAN HERPESVIRUS 3* INFECTIONS:** varicella (chickenpox; vesicular rash; case-fatality rate 9/100,000, with 80% in adults), zoster (shingles), abortion, encephalitis, Guillain-Barré syndrome, non-pyogenic meningitis, pneumonia (including

diffuse interstitial) with exanthem, pneumonitis, retinochoroiditis, anterior uveitis, nonpurulent conjunctivitis, iridocyclitis, iritis, keratoconjunctivitis, arthritis, hepatitis (adult, perinatal and prenatal), mouth lesions, myocarditis and pericarditis, oophoritis, prenatal generalised disease, 1/3 of ischemic strokes in children, Ramsay Hunt syndrome (reactivation of latent virus in geniculate ganglion in immunocompromised patients, causing vesicles over pinna and external auditory meatus, facial nerve palsy, tinnitus, vertigo and deafness); uncommonly, gastrointestinal visceral motor manifestations; transmission by respiratory droplets, crusts from lesions; chickenpox 0.4% of new episodes of illness in UK, herpes zoster 0.4%; herpes zoster affects 10-20% of general population throughout lifetime; chickenpox latent period 8-12 d, incubation period 13-17 d, infectious period 10-11 d, interepidemic period 2-4 y

Diagnosis: Tzanck smear; complement fixation test, ELISA, fluorescent antibody staining, radioimmunoassay; tissue culture of scrapings from skin lesions, vesicle fluid, sputum (lung, liver, spleen post mortem)

Test for Susceptibility: fluorescent antibody to membrane antigen test

Treatment:

Varicella (Chicken Pox):

Immunocompromised, Normal Patient with Pneumonitis or Encephalitis: aciclovir 10 mg/kg i.v. every 8 h for 7-10 d

Immunocompetent Children (< 12 y):

Primary Cases: symptomatic treatment with acetaminophen and antiprurutics

Secondary Cases: aciclovir 20 mg/kg orally 4 times a day for 5 d, starting within 24 h of rash onset

Adolescents and Young Adults: aciclovir 800 mg orally 4-5 times daily for 5-10 d, starting therapy within 24 h of rash onset

Pregnant Women: aciclovir 10 mg/kg i.v. every 8 h

AIDS: famciclovir 500 mg orally 8 hourly for 7-14 d, valaciclovir 1 g orally 8 hourly for 7-14 d, aciclovir 800 mg orally 5 times daily or 10 mg/kg i.v. 8 hourly for 1-2 w (adjust dose for renal function)

Zoster (Shingles; Ophthalmic Zoster, Immunocompromised Patient, Any Patient Seen Within 72 h of Onset of Vesicles): famciclovir 250 mg orally 8 hourly for 7 d (500 mg orally 8 hourly for 10 d in immunocompromised), valaciclovir 1 g orally 8 hourly for 7 d, aciclovir 20 mg/kg to 800 mg orally 5 times daily for 7 d (preferred in children and pregnancy)

Prophylaxis: varicella-zoster immune globulin; supplies limited; administration limited to patient with leukemia, lymphoma, congenital or acquired immunodeficiency, < 24 mo after hematopoietic stem cell transplant or on immunosuppressive therapy or with chronic graft-versus-host disease, with exposure to chickenpox or herpes zoster patient who was household contact, playmate contact of a fairly close nature or hospital contact in adjacent bed, with negative or unknown prior history of chickenpox (except patients who have bone marrow transplantation), and aged < 15 y or adult with good evidence of not having been infected previously, or neonate whose mother had onset of chickenpox within a period of 5 d before and 2 d after delivery; in either case, must be < 96 h after exposure; dose 1 vial/10 kg body weight up to maximum 5 vials; no evidence of beneficial effect against established infection or fetal infection (ie., exposure of women in early pregnancy); immunodeficient patients, especially children, with a negative or unknown history of chickenpox, should be tested for serum antibody to *simplexvirus 3*, thus avoiding unnecessary varicella-zoster immunoglobulin in the future; isolation of cases; live attenuated varicella vaccine gives protection rate of 44-100% and should be given to all susceptible health care workers, household contacts and family members ≥ 12 mo and not pregnant or immunocompromised

***SIMPLEXVIRUS* INFECTIONS:** non-purulent conjunctivitis, iritis, keratoconjunctivitis, anterior uveitis, retinochoroiditis, encephalitis, non-pyogenic meningitis, meningoencephalitis, hepatitis (adult, neonatal and prenatal), localised skin lesions, papulovesicular rash (neonatal), acute herpetic gingivostomatitis, esophagitis, genital herpes, balanitis, nonpurulent cervicitis, urethritis, proctitis, vaginitis, dysuria without frequency, urinary infection, perinatal and prenatal genital disease, arthritis, rhabdomyolysis, acute exudative tonsillitis, pneumonia (neonatal and diffuse interstitial in T cell deficiency) with exanthem, disseminated infection associated with atopic eczema in children

Diagnosis: culture by MRC-5 shell vial centrifugation enhancement and direct immunoperoxidase staining of material from vesicle fluid, throat swab, CSF, corneal scraping, brain post mortem; electron microscopy; indirect fluorescent antibody test for IgM; ELISA (types 1 and 2); complement fixation test, neutralisation antibody titre

Treatment: famciclovir 500 mg orally 12 hourly for 7-10 d, valaciclovir 500 mg orally 12 hourly for 7-10 d, aciclovir 200 mg orally 5 times daily for 7-10 d

Frequent, Severe Recurrences: famiclovir 500 mg orally 12 hourly, valaciclovir 500 mg orally 12 hourly, aciclovir 200 mg orally 8 hourly or 400 mg orally 12 hourly

Prophylaxis (Bone Marrow Transplantation): aciclovir 200 mg 6 hourly from 8 d before to 35 d after bone marrow transplantation

RUBELLA (GERMAN MEASLES): 376 notified cases in Australia in 1999 (steady decrease from 4590 cases in 1995), 271 in USA (58,000 in 1969; 86% in adults in 1999); 0.1% of new episodes of illness in UK; epidemic, worldwide; attack rate 5%;

respiratory transmission; incubation period 2-3 w, latent period 7-14 d, infectious period 11-12 d, interepidemic period 2-7 y; up to 90% of infants born to mothers infected during first 11 w of gestation develop congenital rubella syndrome but the risk falls rapidly from this point

Agent: *human rubella virus*

Diagnosis: 20-50% asymptomatic; incubation period 12-23 d; infectious period 7 d before to 5-7 d after rash onset; infants infected in utero can shed for 1 y or more; conjunctivitis ±, pharyngitis ±, rhinitis ±, exanthem (generalised maculopapular or erythematous rash) ±, postauricular, suboccipital and cervical lymphadenopathy, low grade fever (> 37.2°); arthralgia and polyarthritis in ≤ 70% of adults and adolescent females; thrombocytopenia feature in children; thrombocytopenic purpura, encephalitis, neuritis and orchitis; EIA capture for IgM (false positives with acute Epstein-Barr virus infection, recent *human cytomegalovirus* infection, *Parvovirus* infection), significant rise in serum rubella IgG, tissue culture of throat swab, nasal swab, urine, blood, cerebrospinal fluid (lung, kidney, bone marrow, spleen, brain, lymph node post mortem), reverse transcriptase PCR

Treatment: non-specific

Prophylaxis: highly effective live vaccine (95% efficacy), encephalitis 0.04/M doses, lifetime immunity, highly cost effective; contraindicated in ≤ 12 mo old, pregnant, patients with neomycin allergy and immunocompromised

MUMPS: acute viral disease of childhood; worldwide; endemic in urban areas; ≈ 180 notified cases/y in Australia (≈ 40% in Victoria); case-fatality rate 2/10,000; encephalitis (1:6000 cases; 0.5-2.3% death rate), non-pyogenic meningitis, meningoencephalitis, hydrocephalus, deafness (may be sudden, unilateral and permanent), demyelating disorders, transverse myelitis, Guillain-Barré syndrome, cerebellar ataxia, pancreatitis, mastitis, myocarditis, oophoritis, orchitis, parotitis, salivary adenitis, neuroretinitis, arthritis; 70% salivary gland (60% parotid, 10% submandibular, 5% submaxillary), 10% CNS (5% symptomatic, 0.02% encephalitis), 1% gonadal in prepubertal, 25% epididymoorchitis and 5% oophoritis in postpubertal; respiratory transmission; incubation period 12-26 d, latent period 12-18 d, infectious period 4-8 d, interepidemic period 2-6 y

Agent: *mumps virus*

Diagnosis: complement fixation test, immunofluorescent antibody test for IgG and IgM, ELISA (IgM), hemadsorption, passive hemagglutination, hemagglutination inhibition antibody technique, neutralisation antibody titre (not routine); culture of blood, saliva, throat swab, secretions from Hansen's duct, CSF, urine (brain, salivary glands post mortem) in monkey or human kidney, chick embryo amnion

Treatment: none effective

Prophylaxis: highly effective (83%) live vaccine; all persons ≥ 12 mo not pregnant or immunocompromised

MONKEYPOX: tropical rainforests of West and Central Africa; sporadic zoonosis in man, occasionally fatal, especially in children; secondary attack rate < 4%

Agent: *monkeypox virus*

Diagnosis: electron microscopy

Treatment: non-specific

Prophylaxis: vaccination with smallpox vaccine for laboratory workers involved with virus

HEMORRHAGIC FEVERS

Agents: black measles, hemorrhagic smallpox, hepatitis A, hepatitis B, hepatitis C, chikungunya fever, Sindbis fever, yellow fever, dengue, Crimean-Congo fever, Omsk fever, Kyanasur Forest disease, West Nile fever, Rift Valley fever, Lassa fever, Argentinian hemorrhagic fever (*Junin arenavirus*), Bolivian hemorrhagic fever (*Machupo virus*), Venezuelan haemorrhagic fever (*guanarito virus*), hemorrhagic fever with renal syndrome, *Marburgvirus*, *Ebola-like viruses*, *Russian spring-summer encephalitis virus*, epidemic typhus fever, tick-bite fever, Rocky Mountain spotted fever, Q fever, *Neisseria meningitidis* septicemia, streptococcal septicemia, staphylococcal septicemia, septicemic plague, *Plasmodium falciparum* (haemoglobinuric falciparum malaria, blackwater fever, bilious haematuric fever, haematuric bilious fever, haematuric fever, haemoglobinuric bilious fever, haemoglobinuric fever, haemoglobinuric malaria, haemoglobinuric malarial fever, melanuric fever, malarial haematuria, malarial haemoglobinuria, West African fever), *Tyrpanosoma brucei rhodesiense*; specific agent not demonstrated in large series of cases

Diagnosis: incubation period < 21 d; fever, myalgia and malaise progressing to multiple organ involvement with evidence of vascular damage and hemorrhage; progressive renal failure, rising blood urea, proteinuria, fluid and electrolyte imbalance, sometimes thrombocytopenia (all viral hemorrhagic fevers); specific clinical presentation and epidemiological features may provide clues; repeated blood films for malaria parasites, trypanosomes and spirochaetes; PCR; ELISA for viral antigen; culture of blood, urine and throat swab; fluorescent antibody; serology

Arenaviral Haemorrhagic Fevers: S America, principally Argentina and Bolivia; acute febrile illness with petechiae on skin and palate (*Junin arenavirus*: vesicles on palate); isolation of virus from throat washings or from blood; also serology

Arthropod-Borne Viral Haemorrhagic Fevers: mainly tropical (not found in Australia); usually serology

Haemoglobinuric Falciparum Malaria: sudden onset of chills and irregular fever, nausea, hemoglobinuria, tender and enlarged liver, jaundice, palpable spleen, very dark urine, kidney failure, severe anemia; death in severe cases; due to combination of low level parasitemia, high antibody level and idiosyncratic, probably drug induced, intravascular hemolysis after exposure to amino-alcohol quinolones

Treatment: supportive +:

Argentinian Fever: postconvalescent plasma

Rickettsia: tetracycline, chloramphenicol

***Neisseria meningitidis*, Streptococci:** penicillin

Plague: gentamicin 4-7.5 mg/kg/d i.v., doxycycline 4 mg/kg to 200 mg i.v. then 2 mg/kg to 100 mg i.v. twice daily (not < 8 y), ciprofloxacin 15 mg/kg to 400 mg i.v. twice daily, chloramphenicol 25 mg/kg i.v. 4 times a day

Malaria: sulphadoxine-pyrimethamine, artemisinin, atovaquone-proguanil

***Tyrpanosoma brucei rhodesiense*:** i.v. suramin 1 w, then i.v. melarsopol

Prophylaxis:

Plague Postexposure: doxycycline 2 mg/kg to 100 mg orally 12 hourly (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly

Neisseria meningitidis: ceftriaxone 250 mg (child 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children)

MEASLES (MORBILLI): of worldwide occurrence but coming rapidly under control in temperate countries; virtually eliminated in USA; ≈ 230 notified cases/y in Australia (steady decrease from 4825 cases in 1994); incidence 256/100,000 in Africa; 0.3% of new episodes of illness in UK; global case-fatality rate 2% (67% pneumonia, 33% encephalitis); > 1.5 M deaths/y worldwide; cross-sex transmission gives increased mortality; latent period 6-9 d, incubation period 11-14 d, infectious period 6-7 d, interepidemic period 2-4 y

Agent:measles virus

Diagnosis: initially malaise, fever, conjunctival injection ++, photophobia, hacking cough without pharyngitis, rhinitis with nasal discharge; enanthem (Koplik's spots) has characteristic appearance of tiny white dots, like grains of salt, and are best seen on the cheek near the second upper molar; the exanthem (cutaneous rash) appears 2 d after the Koplik's spots, is initially macular, becomes maculopapular and multiform and may become confluent over face and trunk; complications include bronchopneumonia, otitis media, encephalitis (1 in 2000), subacute sclerosing panencephalitis, hepatitis; epidemiological; culture of throat swab or washings collected soon after rash appears (brain, lung post mortem); serology (capillary blood filter paper specimens suitable (sensitivity 100%, specificity 96%); hemagglutination inhibition (4-fold rise), complement fixation test (titre = 8 at 9 d after onset), staphylococcal protein A adsorption (specific IgM; sensitivity 71%, specificity 81%, predictive value of positive 94%; detected shortly after appearance of rash, peaks within 10 d, usually undetectable by 30 d), sucrose gradient ultracentrifugation, ELISA (IgG, IgM), fluorescent antibody staining (not routine; serum: IgG 96-97% correlation with complement fixation test or hemagglutination inhibition, IgM detected in only ≈ 30%; CSF), neutralisation antibody titre (not routine); confirmatory rather than ruling out); histology (giant multinuclear cells of Warthin-Finkedy type in submucous lymphoid tissue of appendix); neutrophilia with thrombocytopenia, panyctopenia; serum creatinine 6.8 mg/dL; white cell count 14,500 in atypical measles

Treatment: supportive; antimicrobial treatment of secondary infection

Prophylaxis: highly effective live vaccine (95-98% efficacy when given during second year of life; ≈ 100% if second dose at primary or secondary school entrance), encephalitis and encephalopathy 1/M doses, subacute sclerosing panencephalitis 0.5-1.1/M doses, lifetime immunity, highly cost effective, contraindicated in ≤ 12 mo old, pregnant, immunocompromised, severe febrile illness (postponed), tuberculosis, caution (facilities for resuscitation) if history of marked reactions to hen's egg (generalised urticaria, swelling of mouth and throat, difficulty in breathing, hypotension, shock) or hypersensitivity to neomycin or polymyxin (vaccine is produced in chick embryo cell culture and contains trace amounts of neomycin and polymyxin), human globulin injections or other antibody-containing blood products within preceding 3 mo (deferred); passive immunity (patients with severe malnutrition in contact with measles patients): immunoglobulin 0.02 mL/kg i.m. within 5 d of contact

SMALLPOX: with measles, killed 90% of New World population 1518-1837; eliminated as natural infection by use of highly effective live vaccine; potential biowarfare agent; transmission respiratory, contact with lesions; incubation period 7-19 d (average 12 d); fatality rate variola major 5-40%, variola minor 0.1-2%

Agent: *variola major virus, variola minor virus*

Diagnosis: sudden onset of influenza-like symptoms (fever, malaise, headache, chills), prostration, severe back pain, anorexia and vomiting, less often abdominal pain, diarrhoea, delirium and convulsions; 2-3 d later, temperature falls and maculopapular rash appears centrifugally on face, neck and distal extremities including palms and soles and then, after a few days, on trunk and sometimes on more proximal extremities; ulcerating lesions also appear in mucous membranes of nose and mouth; skin lesions progress from macules to papules to vesicles to pustules, which, on the eighth or ninth day, form

scabs which leave depressed, depigmented scabs on healing; rarely, rash accompanied by hemorrhage into mucous membranes and skin (hemorrhagic smallpox; invariably fatal) or lesions fail to form pustules but remain soft and flat (malignant smallpox; almost invariably fatal); complement fixation test, fluorescent antibody staining (not routine), hemagglutination antibody technique; tissue culture of scrapings from skin lesions, vesicle fluid, pus, blood, crust (liver, spleen, blood post mortem)

Treatment: cidofovir 5 mg/kg i.v. weekly for 2 w

Prophylaxis: vaccine up to 4 d (possibly 7 d) after exposure can prevent infection or ameliorate severity (+ vaccine immune globulin in pregnant women and patients with eczema); vaccine containing live *vaccinia virus* protects for at least 10 y; contraindicated for pregnant, persons with diseases or conditions or treatments which cause immunodeficiency or immunosuppression, with a history of eczema, atopic dermatitis or other acute, chronic or exfoliative skin conditions, with previous allergic reaction to smallpox vaccine or life-threatening allergy to polymyxin B sulphate, streptomycin sulphate, tetracycline hydrochloride or neomycin sulphate, with moderate or severe acute illness, < 12 mo old or > 18 y except in emergency, breastfeeding; complications include postvaccinial encephalitis, progressive vaccinia, eczema vaccinatum and generalised vaccinia; vaccinia immune globulin may be given with vaccine to reduce complications or as therapy for complications but is in short supply and should be reserved for most serious cases; cidofovir may be used when vaccinia immune globulin is not efficacious

YELLOW FEVER: transmitted by bite of infected mosquito; incubation period 3-6 d; sylvatic fever in tropical areas of S America (Bolivia, Brazil, Colombia, Ecuador, Peru), sylvatic and urban forms in Africa (endemic in Burkina Faso, Gambia, Ghana, Nigeria, Sudan, Zaire); 5000 cases/y worldwide; no notifications in Australia in past decade

Agent: *yellow fever virus*

Diagnosis: clinically inapparent infections common; overt attacks most common in aged; incubation period 3-6 d; acute onset and constitutional symptoms, followed by brief remission and recurrence of fever, hepatitis, albuminuria and symptoms and, in some instances, renal failure, shock and generalised hemorrhages; severe jaundice in 100%, abrupt onset of chills and fever in 96%, headache in 90%, myalgias in 75%, vomiting in 70%, palatal petechiae in 70%, black vomit in 20%, abdominal pain; raised bilirubin, proteinuria, neutropenia, anemia, thrombocytopenia, reduced levels of coagulation factors; geographic history; vaccination none or > 10 y; exposure to mosquitos; serology (specific IgM or fourfold or greater rise in titre by complement fixation test, hemagglutination inhibition antibody technique, neutralisation antibody titre); demonstration of virus, antigen or genome in tissue, blood or other body fluid; histology of liver (early ballooning and fatty infiltration of hepatocytes, followed by midzonal acidophil necrosis and 'Councilman' bodies within hepatocytes)

Treatment: tiazofurin 825 mg/m^2 for 10 d

Prophylaxis: immunisation administration limited to designated national centres and designated medical practitioners, contraindicated in children < 6 mo, pregnant women (may be reviewed), patients with altered immune status, patients allergic to eggs, should not be administered within 3 w of cholera vaccine

Prevention and Control: mosquito control

DENGUE: transmitted by *Aedes aegypti* mosquito bite; incubation period 3-15 d; all tropical environments, with concentration in Asia, Central and South America; ≈ 60 notified cases/y in Australia (≈ 50% in Queensland; all imported; 43% from Papua New Guinea; causes 8% of fever in returned travellers); global incidence dengue 50-100 M/y, dengue hemorrhagic fever 250,000-500,000/y (24,000 deaths/y); case-fatality rate 3-20%

Agent: *dengue virus* group

Diagnosis: severe myalgia in 100%, arthralgia in 90%, retroocular pain in 75%, nausea in 75%, maculopapular rash in 30%, headache; viral culture of serum or autopsy samples (sensitivity 30-80%), ELISA (IgM positive in 80% by fifth day) on tissue, serum or CSF, immunochromatographic card test (sensitivity 99% in primary cases, 94% in secondary, specificity 93%), reverse transcription-polymerase chain reaction, hybridisation assay (in evaluation), fourfold or greater increase in serum IgG by hemagglutination inhibition test or increase in specific IgM antibody; neutropenia and thrombocytopenia, anemia, hemoglobin 16.6 g/dL, platelet dysfunction, reduced levels of coagulation factors, disseminated intravascular coagulation, vascular injury

Dengue Hemorrhagic Fever

Grade I: fever, constitutional symptoms, positive tourniquet test (≥ 20 petechiae/cm^2), hemoconcentration (rise in hematocrit of ≥ 20%), thrombocytopenia (platelet count < 100,000/μL)

Grade II: Grade I + spontaneous bleeding (eg, skin, gums, gastrointestinal tract)

Grade III (Dengue Shock Syndrome): Grade II + circulatory failure, agitation, hypotension (systolic pressure < 80 mm Hg for those < 5 y or <90 mm Hg for those ≥ 5 y) or narrowing of pulse pressure to < 20 mmHg

Grade IV (Dengue Shock Syndrome): profound shock (blood pressure = 0)

Differential Diagnosis: Chikungunya virus, Hantavirus, measles, rubella, enteroviruses, influenza, hepatitis A, meningococcemia, scarlet fever, typhoid, leptospirosis, rickettsioses, malaria

Treatment: rapid volume replacement through intravenous electrolyte solutions, plasma or plasma expanders (lowers mortality from 10-20% to ≈ 3%)
Prevention and Control: vector control; live vaccine in development
Crimean-Congo hemorrhagic Fever (Central Asian Hemorrhagic Fever): case-fatality rate 10-50%; Europe, Africa, Asia; source tick, nosocomial (person-to-person aerosol), during slaughter of domestic animals; incubation period 2-9 d
Agent: Nairovirus
Diagnosis: hemorrhage predominant; non-purulent conjunctivitis, hemoptysis, meningoencephalitis; disseminated intravascular coagulation in fatal cases; isolation of virus from blood; fourfold rise in antibody titre, presence and decline of IgM antibody; fibrin degradation products > 40 mg/L, platelet count < 10,000/μL, white cell count 4000-7000/μL, reduced levels of coagulation factors, disseminated intravascular coagulation, vascular injury
Treatment: ribavirin
Omsk Hemorrhagic Fever: former Soviet Union, Romania; tick source
Agent: *Omsk haemorrhagic fever virus*
Diagnosis: clinical; thrombocytopenia
Treatment: non-specific
Kyasanur Forest Disease: India; tick source
Agent: *Kyasanur Forest disease virus*
Diagnosis: clinical; thrombocytopenia
Treatment: non-specific
Rift Valley Fever: usually complete recovery in 2 w but retinitis in 10%, hemorrhagic fever in 1% and encephalitis in 1%; case-fatality rate among severely ill > 50% (1% overall); Sub-Saharan Africa, Saudi Arabia, Yemen; sources several *Aedes* and *Culex* mosquitoes, slaughter of domestic animals (camels, cattle, goats, sheep)
Agent: Rift Valley fever virus
Diagnosis: anorexia, 'saddle back' fever, headache, myalgia, retroorbital pain, retinitis with characteristic cotton-wool exudates on macula in 10%, hemorrhage and jaundice (often with death from hepatic failure shock), meningoencephalitis (high death rate); thrombocytopenia, reduced levels of coagulation factors, severe liver dysfunction; serology; isolation by tissue culture or inoculation of suckling mice during acute febrile stage
Treatment: supportive; ribavirin
Prophylaxis: limiting contact with infected mosquitoes, livestock and freshly slaughtered meat
Lassa Fever: widely distributed over W and Central Africa in Guinea, Liberia, Mali, Senegal, Sierra Leone; case-fatality rate 10%; rodent source, nosocomial transmission (person-to-person aerosol)
Agent: Lassa virus
Diagnosis: usually clinical (fever, pharyngitis, retrosternal pain, proteinuria; incubation period 6-21 d) and excluding malaria and diabetic coma, as laboratory tests dangerous; thrombocytopenia, platelet dysfunction, reduced levels of coagulation factors; isolation from blood, throat or urine; serology (fluorescent antibody staining of conjunctival scrapings)
Treatment: ribavirin 30 mg/kg i.v. loading dose, followed by 15 mg/kg i.v. 6 hourly for 4 d, then 8 mg/kg 8 hourly for 6 d
Prophylaxis: ribavirin 500 mg orally every 6 h for 7 d; experimental vaccine
Argentinian Hemorrhagic Fever: Argentina; rodent source, nosocomial transmission
Agent: *Junin arenavirus*
Diagnosis: incubation period 7-16 d; thrombocytopenia, reduced levels of coagulation factors, vascular injury, disseminated intravascular coagulation in terminal shock; serology
Treatment: convalescent antisera; ribavirin
Bolivian Haemorrhagic Fever: Bolivia; rodent source, nosocomial transmission
Agent: *Machupo virus*
Diagnosis: incubation period 7-16 d; thrombocytopenia; serology
Treatment: supportive
Hemorrhagic Fever With Renal Syndrome (Korean Hemorrhagic Fever): Europe, Asia, Americas, Africa; rodents, bats, birds reservoir; transmission via aerosol; person-person transmission reported; ≈ 150,000 hospitalised cases/y worldwide; fatality rate 3-15%
Agent: *Hantavirus*
Diagnosis: incubation period 5-42 d; fever in 94-99%, thirst in 89%, chills in 77-92%, anorexia in 66-96%, nausea in 61-84%, pharyngeal or palatal injection in 55-70%, backache in 53-95%, insomnia in 51%, headache in 42-86%, myalgia in 38-78%, vomiting in 33-70%, epistaxis in 28%, hemorrhages in 26-72%, abdominal pain in 21-66%, constipation in 19-60%, conjunctival injection in 16-79%, dizziness and vertigo in 7-100%, petechiae in 1-99% (mainly in febrile phase); Hantavirus pulmonary infection rare but deadly infection with predominance in the Southwest of USA; creatinine increased in 96%,

C-reactive protein increased in 96%, proteinuria in 94-96%, lactate dehydrogenase increased in 88%, fibrinogen increased in 85%, erythrocyte sedimentation rate increased in 84% (> 20 mm/h in 7-72%), hematuria in 73-86%, albumin decreased in 66%, polyuria in 63-97%, alanine aminotransferase increased in 60%, thrombocytopenia in 52-78%, ASAT increased in 52%, blood urea nitrogen > 20 or serum creatinine level > 2 mg/dL in 50-100%, leucocytosis in 41-92%, oliguria in 37-83%, hypotension in 22-80%, disseminated intravascular coagulation in 5%, platelet dysfunction, reduced levels of coagulation factors, prolonged prothrombin time, vascular injury; immunofluorescent antibody test, ELISA

Treatment: ribavirin 30 mg/kg i.v. then 15 mg/kg i.v. 6 hourly; fluids, vasopressors, dialysis, plasma and platelet transfusions

Prophylaxis: combined *Hantavirus/Puumula virus* vaccine

Nephropathica Epidemica: mild form of hemorrhagic fever with renal syndrome occurring in Scandinavia

Agent: *Puumala virus*

Diagnosis: acute onset of symptoms in all cases, fever in 99-100%, thirst in 89%, headache in 85-90%, backache in 82-84%, nausea in 78-84%, vomiting in 70%, myalgia in 69%, abdominal pain in 67%, anorexia in 66-70%, chills in 60%, insomnia in 51%, petechiae in throat and soft palate in 36%, conjunctival injection in 18%, petechial rash in 12%, epistaxis in 10%; proteinuria in all cases, C-reactive protein raised in 96%, lactate dehydrogenase raised in 88%, bleeding time normal in 86%, erythrocyte sedimentation rate raised (> 20 mm/h) in 84-90%, thrombocytopenia in 80%, whole blood coagulation time normal in 77%, Rumpel-Leede tourniquet test normal in 77%, hematuria in 74%, blood urea nitrogen > 20 or serum creatinine level > 2 mg/dL in 70-96%, serum albumin decreased in 66%, alanine aminotransferase increased in 52%, prothrombin ratio normal in 50-60%, leucocytosis in 37%; serology; histology (hemorrhages in renal medullary interstitium in all cases, hemorrhages in renal cortex in 53%)

Treatment: as for **Hemorrhagic Fever with Renal Syndrome**

Marburg Hemorrhagic Fever: Kenya and Republic of South Africa; source unknown, nosocomial transmission (person-to-person aerosol); high mortality

Agent: *Marburgvirus*

Diagnosis: incubation period 3-9 d; disseminated intravascular coagulation in fatal cases; virus specific immunofluorescence or electron microscopy of isolate (grows readily in Vero cells) from blood or serum or suspensions of heart, kidney, liver or spleen, histology and electron microscopy of autopsy specimens (liver and kidney tissue); complement fixation test less sensitive than indirect fluorescent antibody titre; IgM peaks 2-3 w after onset; IgG rises more slowly and may be found in low titres years later; leucopoenia (1400/μL), relative lymphocytosis, atypical monocytes, thrombocytopenia, reduced levels of coagulation factors, disseminated intravascular coagulation; occult blood in stool, elevated serum transaminases, alkaline phosphatase, amylase and bilirubin

Treatment: supportive

Ebola Hemorrhagic Fever (African Hemorrhagic Fever): case-fatality rate 50-90%; Central and E Africa, Sudan; source unknown, nosocomial transmission (person-to-person aerosol); acute febrile systemic infection

Agent: *Ebola-like viruses*

Diagnosis: incubation period 2-21 d; fever, extreme asthenia, gastroenteritis with diarrhoea, nausea and vomiting, headache, arthralgias, back pain, myalgias; bilateral conjunctival injection, maculopapular rash and pharyngitis with severe odynophagia in patients prone to hemorrhagic manifestations; antibody ELISA (IgG and/or IgM), virus isolation, immunohistochemistry of skin biopsy, reverse transcriptase polymerase chain reaction; thrombocytopenia, reduced levels of coagulation factors

Treatment: supportive

Ross River Fever (Epidemic Polyarthritis): endemic in Australia (≈ 4000 notified cases/y (≈ 52% in Queensland)), New Guinea, Solomon Islands; mosquito vector

Agent: Ross River virus

Diagnosis: polyarthralgia, rash, malaise, myalgia, fever; culture of serum; ELISA (IgG and IgM)

Treatment: non-specific

Barmah Forest Virus Infection: widespread in Eastern states of Australia (≈ 600 cases/y, ≈ 50% in Queensland)

Agent: Barmah Forest virus

Diagnosis: rash in 80-90%, fever in 60-80%, arthritis or arthralgia in 50%, headache in 40-50%, respiratory symptoms in 20%, gastrointestinal symptoms in 15%; serology

Treatment: non-specific

Phlebotomus Fever (Sandfly Fever)

Agent: *Phlebovirus*

Diagnosis: serology

Treatment: supportive

Prophylaxis: ribavirin

MUCOCUTANEOUS LYMPH NODE SYNDROME (KAWASAKI DISEASE, KAWASAKI SYNDROME): acute, febrile, exanthematous infectious disease (mucocutaneous, lymph node inflammation and systemic vascular disease); worldwide but unusual, affecting mainly children; attack rate 7/100,000 in children < 5 y, 0.4/100,000 in Caucasian, and 2.7/100,000 in Oriental, children < 8 y; case-fatality rate 1-2% (cardiac involvement); several cases found in Australia; vector ? house mites and cat fleas

Agent: ? *Ehrlichia*, ? retrovirus

Diagnosis: rash (macular, papular, polymorphous, scarlatiniform, urticarial, vesicular, erythema multiforme) in 100% of cases (erythema multiforme rash without vesicles or crusts in 90%), ≥ 5 d of fever in 95%, desquamation of fingertips in 85-95%, bilateral conjunctival injection in 81-90%, dryness of lips in 80%, non-suppurative lymphadenopathy in 75-85%, indurative edema of hands or feet in 75%, desquamation of palms and soles in 73%, red oropharynx in 73%, carditis in 70%, periungual desquamation in 69%, other desquamation in 58%, redness and fissuring of lips in 66-90%, coronary artery abnormalities in 23% (cardiac arteries may be affected by widespread endarteritis, resulting in aneurism formation, thrombosis or rupture, causing death in third or fourth week; even those apparently not affected may develop highly premature coronary artery disease in later life), diarrhoea, arthralgias/arthritis, aseptic meningitis, mild jaundice, transient nail furrow 1-2 mo post-onset; electrocardiogram (transient changes associated with diffuse ischemia or myocarditis in 11% of cases, myocardial infarction in 4-8%, increased PR interval, increased ST interval, decreased R waves, flat T waves); raised erythrocyte sedimentation rate, platelet count increased days 10-25; white cell count increased in 68% (shift to left), proteinuria and increased urinary leucocytes in 46%, slight anemia in 44%, slight elevation in serum transaminases in 19%

Differential Diagnosis: infectious mononucleosis, leptospirosis, scarlet fever, serum sickness, systemic lupus erythematosus, rubella, measles, Rocky Mountain spotted fever, scalded skin syndrome, juvenile rheumatoid arthritis, staphylococcal toxic shock

Treatment: aspirin 60-100 mg/kg daily in divided doses, then 10-30 mg/kg daily for 6-8 w (reduces incidence of aneurisms) + γ-globulin 400 mg/kg/d i.v.; PGE_1 or sympathetic block + thrombolytic and anticoagulant therapies in peripheral ischemia

REYE SYNDROME: case-fatality rate 23-30%; age of onset 4 d-29 y (usually 6 mo-15 y; 95% age < 14 y), 94% Caucasian, 55% antecedent respiratory illness, 25% varicella, 10% diarrhoea; permanent neurological or psychiatric disorders in 34-61% of survivors

Agents: interaction of aspirin and other salicylates with *influenza A virus, influenza B virus, simplexvirus 3* (5-30%) and other viruses

Diagnosis: history of viral infection; encephalopathy, varying from drowsiness to deep coma (also combativeness, confusion), associated with vomiting and hepatic enlargement; no evidence of drug intoxication; no jaundice (slightly elevated or normal serum bilirubin), but ≥ 3 fold rise in serum transaminases and serum ammonia levels, and there may be hypoglycemia (only in children < 5 y) and disturbances of acid-base balance and of blood clotting (prolonged prothrombin time); CSF < 8 leucocytes/μL; cerebral edema without perivascular or meningeal irritation; histologically (biopsy or autopsy), liver shows microvesicular fatty metamorphosis, with fine droplets of fat scattered through cytoplasm of hepatocytes; electron microscopy shows specific mitochondrial damage which is self-limiting

Treatment: supportive

MULTISYSTEM *STREPTOCOCCUS PYOGENES* DISEASE: in children; preexisting varicella in 47%; also associated with use of nonsteroidal antiinflammatory drugs

Agent: *Streptococcus pyogenes*

Diagnosis: confusion in 62% of cases, abdominal pain in 62%, headache/irritability in 50%, vomiting in 50%, anorexia in 50%, local extremity swelling/pain in 50%, hyperesthesia in 50%; hypoalbuminemia in 100%, renal sediment abnormalities in 100%, elevated immature polymorphonuclears in 87%, hyponatremia in 87%, lymphopenia in 75%, elevated AST in 67%, thrombocytopenia in 62%, prothrombin time > 14 s in 60%, fibrin split products or fibrinogen < 500 in 60%, elevated creatinine in 50%, direct hyperbilirubinemia in 50%; blood cultures

Treatment: benzylpenicillin 150,000-200,000 U/kg i.v. daily in divided doses

LISTERIOSIS (LISTERELLOSIS, LISTEROSIS): ≈ 50 notified cases/y in Australia; ≈ 30 cases/y in USA (50% nosocomial), 56% of isolates from blood, 16% blood and CSF; bacteremia without known focus (43% of infections), cutaneous listeriosis, disseminated (typhoidal) listeriosis, food poisoning (from unpasteurised or inadequately pasteurised milk, fresh soft cheeses, ready to eat deli meats and hot dogs), genital tract listeriosis, listerial endocarditis (endocardial listeriosis), listerial meningoencephalitis (meningitis/meningoencephalitis 43% of infections; associated with malignancy; also, neonatal and postneonatal pyogenic meningitis), listerial septicemia, lymph gland infections, neonatal disseminated listeriosis, oculoglandular listeriosis, prenatal generalised disease; case-fatality rate from 0% in previously healthy patients to 80% in disseminated infection; fatal neonatal listeriosis 0.1-0.3% of births, 1-7% of perinatal deaths; risk factors pregnancy, neonatal status, hematological, gastrointestinal or pulmonary malignancy, organ transplantation, oncologic chemotherapy, steroid therapy, systemic lupus erythematosus, alcoholism, renal failure, hepatic failure, portal hypertension and ascites, increased age, splenectomy, *human immunodeficiency virus* infection

Agent: *Listeria monocytogenes*

Diagnosis: incubation period 9-48 h for gastrointestinal symptoms, 2-6 w for invasive disease; fever, muscle aches and nausea or diarrhoea; pregnant women may have mild flu-like illness (fever in 82%, chills in 82%, headache in 82%, abdominal cramps in 45%, stiff neck in 45%, vomiting in 27%, photophobia in 18%) and infection can lead to premature delivery or stillbirth

Disseminated: granulomatous lesions and focal necroses; elderly or immunocompromised may have bacteremia or meningitis

for other forms, see appropriate sections

culture of appropriate specimen on blood agar; cold enrichment at 4°C may be useful in some circumstances; blood or CSF cultures; antibody to listerolysin O may be helpful to identify outbreak retrospectively

Treatment: supportive care + i.v. ampicillin, penicillin or cotrimoxazole

ACTINOMYCOSIS: cervicofacial (lumpy jaw; most common form; usually arising as result of infection following extraction of tooth or injury to jaw), pulmonary (arises from inhalation or aspiration of infective material (eg., from cervicofacial lesions), by extension of abdominal disease or, more rarely, by metastasis of disseminated disease), abdominal (gastrointestinal actinomycosis; most common in ileorectal region but sometimes in anorectal or gastric areas; arises from intestinal flora and intestinal perforation), septicemia (usually from pulmonary), brain, bone, liver, kidney, genital (uterus, associated with intrauterine devices), disseminated; ≈ 6 cases/y in USA; endogenous (oral)

Agents: *Actinomyces israelii, Actinomyces naeslundii, Actinomyces odontolyticus, Actinomyces meyeri, Actinomyces bovis, Propionibacterium propionicum, Bifidobacterium*

Diagnosis: visualisation of macroscopic sulphur-coloured colonies in pus; Gram stain, direct immunofluorescent stain and anerobic culture of pus, curettings, biopsy from wall of abscess; neutrophilia and raised erythrocyte sedimentation rate usual

Cervicofacial: painful swelling on jaw that enlarges and eventually forms sinuses that open onto cheek or submandibular region

Abdominal: abdominal discomfort, fever, palpable mass, production of external sinus

Pulmonary: severe pneumonia, lung abscess or empyema, with characteristic production of small, multiple abscesses and sinuses in chest wall; on occasion, actinomycotic pneumonia may simulate a pulmonary neoplasm or tuberculosis

Treatment: penicillin (mild disease: phenoxymethylpenicillin 500 mg 6 hourly (< 12 y: 25-50 mg/kg daily orally in 4 divided doses); severe disease: benzylpenicillin 10M units (children: 100 000-250 000 U/kg) daily i.v. in 4 divided doses for 6 w, then phenoxymethylpenicillin as above), tetracycline 500 mg 6 hourly orally for 6 weeks, erythromycin 500 mg 4 times daily (children: 30 mg/kg daily in 4 divided doses) orally for 6 w

Prophylaxis: good dental hygiene

ANTHRAX (CONTAGIOUS ANTHRAX, FELLMONGER'S DISEASE, TANNER'S DISEASE): an acute disease of herbivorous animals readily transmitted to man; worldwide; rare in Australia

Agent: *Bacillus anthracis*

Diagnosis: Gam positive bacilli seen on microscopy; confirmed by culture; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test

Treatment: see **CUTANEOUS ANTHRAX, PULMONARY ANTHRAX, GASTROINTESTINAL ANTHRAX, MENINGITIS, BACTEREMIA**

Prophylaxis: vaccine 93% effective against cutaneous form, effectiveness against other forms not known

Prevention and Control: sterilisation of infected tissue, hides, etc

NOCARDIOSIS: worldwide; 70 cases (≈ 20 deaths)/y in USA; associated with Hodgkin's disease, connective tissue disorders, diseases treated by organ transplantation and corticosteroid administration; 75% lungs (33% only; may simulate pulmonary tuberculosis; subacute chronic pneumonia, occasionally with extension to pleura, resulting in empyema (pulmonary mycetoma) and dissemination), 23% brain, meninges and spinal cord; skin and subcutaneous tissue lesions ± osteomyelitis, kidneys, adrenals, eye, liver, lymph nodes, pericardium, myocardium (disseminated disease); lymphocutaneous (may present similarly to sporotrichosis, most commonly *Nocardia brasiliensis*); actinomycetoma (usually lower extremity secondary to trauma); septic arthritis; disseminated; epididymoorchitis (extremely rare)

Agents: *Nocardia asteroides*, *Nocardia brasiliensis*, *Nocardia brevicatena, Nocardia ototididiscaviarum, Nocardia farcinica, Nocardia nova*

Diagnosis: Gram (Brown-Breen or Hueker modification) and Ziehl-Neelsen (Kinyoun or Putt modification) stains and culture of sputum, thoracentesis specimen, transtracheal aspirate, bronchial brushings, lung biopsy, pus from abscess or draining sinus, biopsy from other affected sites; serology (immunodiffusion)

Treatment: cotrimoxazole 320/1600 mg orally 12 hourly (child: 6/30 mg/kg daily in 2 divided doses) for 6-12 mo; sulphadiazine 100 mg/kg orally daily in 4 divided doses (child: 75 mg/kg initially, then 160 mg/kg daily in 4-6 divided doses to 6 g daily) + sodium bicarbonate 50 mg/kg orally daily in 4 divided doses for 4-6 w, then sulphisoxazole 60 mg/kg 6 g orally daily in divided doses for 12-18 mo; minocycline 300 mg orally 12 hourly; ciprofloxacin, cefotaxime, amikacin, imipenem, linezolid; surgical excision or drainage of abscesses, empyema and other necrotic tissue

TUBERCULOSIS: progressive or chronic disease; usually begins in lung but may affect any other organ or system, eg., lymphatic, osseous, urogenital, nervous and gastrointestinal systems and skin; conditions caused include tuberculous laryngitis (laryngeal tuberculosis), lymphadenitis (tuberculosis of intrathoracic lymph nodes, tuberculous peripheral lymphangitis), meningitis, leptomeningitis, meningoencephalitis, brain abscess, myelitis, ascites, peritonitis (peritoneal tuberculosis, tuberculosis of the peritoneum), arthritis, osteitis, osteomyelitis, synovitis, tenosynovitis, kyphosis (Pott curvature), spondylitis, dactylitis, mastoiditis, pyelitis, pyelonephritis, epididymitis, oophoritis, salpingitis, erythema nodosum, adenitis, episcleritis, interstitial keratitis, keratoconjunctivitis, otitis media, Addison disease, mediastinal tuberculosis (tuberculosis of the mediastinum), nasal tuberculosis, nasopharyngeal tuberculosis (tuberculosis of the nasopharynx), pharyngeal tuberculosis, cerebral tuberculosis (tuberculosis of the brain), intestinal tuberculosis (tuberculosis of the intestine, tuberculous enteritis), rectal tuberculosis, anorectal tuberculosis, anal tuberculosis, spinal tuberculosis (David disease, Pott caries, tuberculosis of the vertebral column, tuberculous spondylitis), tuberculosis of the hilar and other lymph nodes, sinuses, ear, mouth, esophagus, liver, genitourinary system, kidney, bladder, ureter, prostate, seminal vesicle, testis, endometrium (tuberculous endometritis), skin and subcutaneous tissues, thyroid gland, adrenal glands, spleen, endocardium, myocardium, pericardium, hip and knee, meningeal tuberculoma; miliary tuberculosis is a disseminated tuberculosis that spreads via lymphatic vessels and bloodstream from any active tuberculous lesion; massive hematogenous spread of bacilli results in tubercles scattered throughout pulmonary tissue and other body tissues (rarely, skin tissue); occurs mainly in elderly and immunocompromised; old foci may be reactivated by alcoholism, anthracosis, corticosteroid therapy, cytotoxic therapy, diabetes mellitus, gastric resection, malignancy, malnutrition, old age, pulmonary infections, radiation, sarcoidosis, severe viral infections, silicosis, thoracic surgery, thoracic trauma; abscesses in liver, abdominal wall, psoas muscle, mediastinum and peripancreatic area common in AIDS (12% of cases of tuberculosis); leading cause of death due to infectious organism worldwide (2 M deaths/y, with 8-10 M new active cases (20% in India); 1.9 billion infected worldwide; ≈ 1000 notified cases/y in Australia (≈ 26% in Victoria; most new cases in migrants from Indochina and South East Asia); 69% pulmonary, 9% lymphatic, 5% pleural, 3% multiple, 2% bone/joint, 1% meningeal, 6% other; ≈ 20,000 cases/y in USA; transmission from elephants to humans recently reported

Agents: *Mycobacterium tuberculosis* (usually acquired by inhalation), *Mycobacterium bovis* (usually acquired by ingestion; 30-40% respiratory; also genitourinary, lymphatic, skeletal and disseminated), *Mycobacterium africanum*

Diagnosis: persistent productive cough, hemoptysis, unexplained fever and night sweats, unexplained weight loss; auramine-rhodamine, Kinyoun or Ziehl-Neelsen stain and Bactec 12B (97% *M.tuberculosis* (mean 14 d) and 94% nontuberculous mycobacteria (mean 13 d) positive; 3% contamination rate), Mycobacterial Growth Indicator Tube (92% *M.tuberculosis* (mean 19 d) and 94% nontuberculous mycobacteria (mean 14 d) positive; 4% contamination) or Septichek AFB biphasic system or routine culture (Middlebrook 7H9, 7H10, 7H11 or selective 7H11 or Lowenstein-Jensen; 95% *M.tuberculosis* (mean 29 d) and 77% nontuberculous mycobacteria (25 d) positive; 4% contamination) of appropriate specimen; tuberculin test (PPD; zone of induration read at 72 h; ≥ 5 mm positive in patients with HIV, close contacts of active TB cases, patients with chest X-ray findings of inactive tuberculosis or fibrosis, patients with organ transplants or other immunosuppression; ≥ 10 mm positive in patients with medical risk factors for TB (silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphoma, carcinoma of head, neck or lung, weight loss of ≥ 10% of ideal body weight, gastrectomy, jejunoileal bypass), injection drug users, immigrants within last 5 y from high prevalence countries, residents and employees of prisons, nursing homes and other long term facilities for elderly, hospitals and other health care facilities, residential facilities for patients with AIDS and homeless shelters, mycobacteriology laboratory personnel, children ≤ 4 y or infants, children and adolescents exposed to adults at high risk; ≥ 15 mm positive in persons with no risk factors for TB; 'true' negative if patient never infected with *Mycobacterium tuberculosis* or if isoniazid prophylaxis begun within 3 mo of skin test conversion; can be 'false' negative (10-25% of active tuberculosis) in small children, early in infection, in acute miliary tuberculosis, tuberculous pleurisy and tuberculous meningitis, if the patient also has *human immunodeficiency virus* infection, measles, mumps, chickenpox, scarlet fever, influenza, typhoid fever, brucellosis, typhus, leprosy, pertussis, South American blastomycosis, chronic lymphocytic leukemia, lymphoma, Hodgkin's disease, sarcoidosis, amyloidosis, uremia, chronic renal failure, severe protein depletion or has received live virus vaccine (measles, mumps, polio) or is on immunosuppressive therapy, in late pregnancy and puerperium, old age and occasionally middle age, if patient has been receiving UV light therapy or sunbathing, in stress states such as surgery, burns, mental illness, graft versus host reactions, and in individuals of low sensitivity or if infected with atypical mycobacteria, also if incorrect dilution of tuberculin, incorrect diluent, improper storage (inactivated by sunlight, heat), adsorbed to container (partially controlled by addition of Tween 80), chemical denaturation, bacterial contamination, injection of too little antigen, delay in administration after drawing of preparation into syringe, injection too deep, incorrect route, improper reading (unsupervised reader, conscious or unconscious bias, error in reading); interferon gamma test; PCR (sensitivity 90%, specificity 99.6%); DNA probe identification; gene amplification and hybridisation or RFLP; ELISPOT; serum angiotensin converting enzyme decrease; rheumatoid factor may be present; 4% of cases diagnosed postmortem

Miliary Tuberculosis: fever in 89-90%, anemia in 78%, sweats in 86%, weight loss in 66%, cough in 55%, weakness in 53%, dyspnoea in 50%, tachypnoea in 47-50%; reticulonodular miliary chest radiograph in 68%; sputum culture positive in 76%, gastric aspirate in 75%, urine in 59%, bronchial washings in 54%

Treatment: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 6 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 6 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (6 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isonazid and rifampicin (to 6 mo); vitamin A and zinc may augment efficacy

Latent Infection (Prophylaxis): rule out active tuberculosis and do not give if previous treatment for TB or previous isoniazid, previous isoniazid adverse reaction or acute or unstable liver disease; otherwise, should be given to recent tuberculin converters; children and adolescents with strongly positive tuberculin reactions; tuberculin positive juvenile close contact; old untreated tuberculosis or radiologically healed pulmonary lesion, tuberculin positive or anergy in patients about to be treated with steroid drugs or by immunosuppressive or chemotoxic therapy or radiotherapy; patients with chronic lung disease such as silicosis; patients with tuberculin skin test > 5 mm who have not had BCG or with positive TB-specific interferon gamma release assay and with cancer or other debilitating disease or with diabetes or chronic renal failure (especially if < 35 y) or who have had a gastrectomy, having long-term corticosteroid therapy or other immunosuppressive therapy (prior to commencement), with history of tuberculosis and with leukemia, Hodgkin's disease or other chronic malignancies, with silicosis and with *human immunodeficiency virus* infection; isoniazid 10 mg/kg to 300 mg orally daily [+ pyridoxine 25 mg (breastfed baby: 5 mg) orally with each dose] for 6-9 mo; vitamin D 2.5 mg single oral dose

Contacts of Isoniazid Resistant, Rifampicin Susceptible TB: rifampicin 10 mg/kg to 600 mg orally daily + pyrazinamide 15-20 mg/kg to 2 g daily for 2 mo

Patients Who Cannot Tolerate Pyrazinamide: rifampicin 10 mg/kg to 600 mg daily for 4 mo

Prophylaxis:

Vaccination: live vaccine (BCG) efficacy 50% total, 66% meningitis, 71% death from TB; ulceration and lymphadenitis in 1-10%, osteomyelitis 1/M vaccinees; duration of immunity unknown, cost effective; recommended for Aboriginal and Torres Strait Islander neonates in regions of high incidence, neonates born to patients with leprosy (cross-protection), children under 5 y who will be travelling to live in countries of high TB prevalence for long periods, neonates who will be living in a household which includes immigrants or visitors recently arrived from countries of high prevalence or who have returned to visit homes of relatives in countries of high prevalence, children and adolescents aged < 16 y who continue to be exposed to a patient with TB and child or adolescent cannot be given isoniazid or where the person with active disease has organisms resistant to both rifampicin and isoniazid; may also be given to healthcare workers in frequent contact with patients with tuberculosis, especially multi-drug resistant tuberculosis; should not be given to patients with current or previous tuberculosis, with a current febrile illness, with skin conditions such as eczema or dermatitis, who have had a previous live vaccination within the past 4 w, with a history of a positive reaction to a Mantoux test, who are HIV positive or are in a high risk group for HIV and have not been tested, or receiving immunosuppressive medication such as corticosteroids or cancer chemotherapy or with other conditions likely to suppress immunity

Infants of Mothers with Active Pulmonary Tuberculosis: isolation for 7-10 d and treatment of cases

MYCOBACTERIOSIS DUE TO *MYCOBACTERIUM KANSASII:* uncommon; clinically indistinguishable from pulmonary tuberculosis (great majority of patients underlying pulmonary factors, 70% nonpulmonary disposing factors), cervical adenitis in children, arthritic and renal lesions reported, disseminated infection (lung, reticuloendothelial system, bone, joint, skin) in severely immunocompromised patients, frequently with pulmonary predispositions

Diagnosis: Ziehl-Neelsen stain and culture of sputum, lymph gland, bone marrow, spleen biopsy; severe anemia, gross leucopoenia (to 500/μL), gross thromobocytopenia; bone marrow severe hypoplasia of hematopoietic cells

Differential Diagnosis: lymphoma, leukemia (blood smear, bone marrow examination)

Treatment: isoniazid 10 mg/kg to 300 mg orally daily + rifampicin 10 mg/kg to 600 mg orally twice daily + ethambutol 15 mg/kg orally (not < 6 y) daily for 18 mo and 12 mo negative cultures

DISSEMINATED MYCOBACTERIOSIS IN AIDS

Agents: *Mycobacterium avium-intracellulare*; also *Mycobacterium tuberculosis*, *Mycobacterium kansasii*, *Mycobacterium gordonae, Mycobacterium fortuitum, Mycobacterium chelonae, Mycobacterium xenopi, Mycobacterium szulgai, Mycobacterium smegmatis, Mycobacterium scrofulaceum, Mycobacterium malmoense, Mycobacterium flavescens, Mycobacterium asiaticum, Mycobacterium bovis, Mycobacterium haemophilum, Mycobacterium genavense*

Diagnosis: fever in 87% of cases, night sweats in 78%; anemia (< 8.5 g hemoglobin/dL) in 85%, elevated serum alkaline phosphatase in 53%; Ziehl-Neelsen stain and culture of lung biopsy (100% positive), spleen biopsy (100% positive), brain biopsy (100% positive), duodenal contents (100% positive), blood (63-86% positive; use Isolator lysis centrifugation concentrate inoculated into a Bactec 7H12 culture vial and onto Wallenstein medium or Bactec 13A broth system), sputum

(56% positive), bronchial washing (50% positive), liver biopsy (43-67% positive), stool (42-100% positive); postmortem histology of lung, lymph node, spleen, bone marrow, brain, adrenals, liver, intestine (all 100% positive)

Treatment (*Mycobacterium avium*):

Initial Regimen: ethambutol 15 mg/kg orally daily (not < 6 y) + clarithromycin 12.5 mg/g to 500 mg orally 12 hourly daily or azithromycin 10 mg/kg to 500 mg orally daily + rifampicin 10 mg/kg to 600 mg orally daily or rifabutin 5 mg/kg to 300 mg orally daily

Salvage Regimen: amikacin 10 mg/kg daily ± ciprofloxacin 750 mg bid

Prophylaxis (CD4 < 50/μL): azithromycin 1.2 g orally weekly, clarithromycin 500 mg twice a day, rifabutin 300 mg orally daily

Disseminated Mycobacteriosis in Non-AIDS Patients: skin involvement in patients with no immune defect, kidney transplant recipients, collagen disease, chronic renal failure, 90% survival rate; widespread, multiorgan involvement, severe illness in cell-mediated immunity deficiency, lymphoma, leukemia, survival rate 10%; intermediately severe illness and response to therapy in patients with other underlying diseases

Agents: *Mycobacterium fortuitum*, *Mycobacterium chelonae;* also *Mycobacterium gordonae*, *Mycobacterium malmoense*

Diagnosis: histology (dimorphic (acute and granulomatous) inflammation) and culture of skin lesions; blood cultures

Treatment:

Mycobacterium fortuitum*, *Mycobacterium chelonae: 2 of clarithromycin, doxycycline, ciprofloxacin, cotrimoxazole orally for 6-12 mo

Mycobacterium gordonae: isoniazid + rifampicin + pyrazinamide

***Mycobacterium malmoense*:** rifabutin + clofazimine + isoniazid

Leprosy (Hansen Disease, Hanseniasis, Lepra, Lepra Arabum, St Lazarus' Disease): usually chronic infectious disease mainly affecting skin, peripheral nerves and mucosa of upper respiratory tract; formerly worldwide, now largely confined to tropics; 600,000 cases worldwide (mainly in Brazil, India, Madagascar, Mozambique, Myanmar, Nepal); 150 cases/y in USA; 6 notified cases in Australia in 1999 (50% in Western Australia); transmission by personal contact; incubation period years

Agent: *Mycobacterium leprae* (? + cooperation of corynebacteria)

Diagnosis: combination of skin lesions and thickening of peripheral nerves very suggestive; leprosy is characterised by a wide variety of lesions; intradermal lepronin aids in assessing type; indeterminate leprosy (indeterminate Hansen disease, indeterminate hanseniasis, lepra incaracteristica, uncharacteristic leprosy, undifferentiated leprosy), the earliest form, is characterised by 1 or more ill-defined and asymptomatic hypopigmented or erythematous lesions with ill-defined borders appearing on face, scapular region, buttocks or extremities; there may be minimal sensory loss in lesions; lesions may be transient and self-healing but may evolve to lepromatous or tuberculoid type; nerve damage does not occur; in tuberculoid leprosy (paucibacillary leprosy, TT leprosy, tuberculoid Hansen disease, tuberculoid hanseniasis), there may be 1 or several well-defined erythematous or brownish red anesthetic or hypesthesic skin lesions appearing on the extremities, trunk, buttocks or face; damage to peripheral nerves is usually severe but limited to the skin lesions and the main nerve trunk related to the main skin lesions; borderline leprosy (B leprosy, BB leprosy, bi-polar leprosy, borderline group, dimorphic leprosy, dimorphous Hansen disease, dimorphous hanseniasis, dimorphous leprosy, intermediate leprosy, mixed leprosy) occupies most of the spectrum between tuberculoid leprosy and lepromatous leprosy; it is unstable and may include a wide range of manifestations of either of the 2 polar forms; nerve damage may be severe, rapidly advancing and unpredictable; it may precede cutaneous manifestations of the disease; borderline leprosy with tuberculoid features (borderline tuberculoid leprosy, BT leprosy) and borderline leprosy with lepromatous features (borderline lepromatous leprosy, BL leprosy) may be distinguished; lepromatous leprosy (diffuse leprosy, elephantiasis graccorum, hanseniasis virchowiana, lepra tuberosa, lepromatous Hansen disease, LL leprosy, multibacillary leprosy, nodular Hansen disease, nodular hanseniasis, nodular leprosy, virchowian hanseniasis) is a progressive form in which skin lesions are bilateral symmetrical, numerous, diffuse, erythematous and ill-defined macules; later, papules, nodules and diffuse infiltrations appear; at a later stage, eyebrows and eyelashes may be lost; involvement of nasal mucosa may lead to crusting, obstructed breathing and epistaxis; collapse of the nose is characteristic of advanced cases; ocular involvement leads to iritis and keratitis; diffuse lepromatous leprosy (diffuse lepromatosis, diffuse leprosy, Lucio leprosy) is a variety in which there is diffuse infiltration of skin but no macules or nodules; eyebrows may be lost and generalised paresthesiae may occur, with bouts of pyrexia; polygonal ulceration of skin occurs, especially near elbows and knees; if reactions develop, patients exhibit necrotising vasculitis (Lucio phenomenon; erythema necroticans, necrotising vasculitis of leprosy) rather than erythema nodosum leprosum; essentially limited to Central America and, especially, certain States in Mexico; neural leprosy = involvement of peripheral nerves in the absence of detectable skin lesions; reactions are acute inflammatory states occurring in any type of leprosy except early or indeterminate and precipitated by a change in the hormonal state (eg., during pregnancy or parturition), pyrexia (however caused), viral infection and smallpox vaccination; reversal reaction (upgrading reaction), occurs in borderline leprosy; preexisting lesions in skin and peripheral nerves become acutely painful, erythematous and inflamed; new lesions may occur; fever usually absent; increase in cell-mediated immunity; erythema nodosum leprosum (ENL, type 2 reaction) occurs in

multibacillary (especially lepromatous) leprosy; crops of red, tender nodules and 'pink patches' appear on trunk, face and exterior surfaces of limbs; usually accompanied by fever and systemic signs, eg., general malaise and pains in large muscle masses, arthralgia (perhaps with effusion into joints), lymphadenopathy, iridocyclitis, neuropathy, orchitis and nephritis; modified Ziehl-Neelsen stain of scrapings from mucosal ulcers or fluid from nodules obtained by scrape-incision method, biopsy of macule, muscle or nerve (bacilli are not found, or are extremely scanty, in indeterminate leprosy, usually very scanty in tuberculoid, easily found in borderline, rather low in borderline tuberculoid, numerous in lesions but absent from apparently normal skin and usually absent from nasal mucosa in borderline lepromatous, and found in large numbers in lesions, apparently normal skin, peripheral nerves, mucosa of the upper respiratory tract, retioculoendothelial system, eyes, testes and bone marrow in lepromatous); histological examination of a lesion; ELISA (antibody); causes moderate anemia, increased serum globulins, reduced serum albumin, raised erythrocyte sedimentation rate, increased serum angiotensin converting enzyme

Neural Leprosy: histopathology usually consistent with tuberculoid or borderline tuberculoid disease

Lucio Phenomenon: histopathologically a necrotising vasculitis with extravasation of erythrocytes and fibroid degeneration of blood vessel walls

Differential Diagnosis: fungal infections, yaws, vitiligo, leishmaniasis, mycoides fungoides, lupus, syphilis, disseminated tuberculosis; tuberculoid leprosy may be histologically indistinguishable from sarcoidosis unless there are changes (lymphocytic and histocytic infiltration) in the cutaneous nerve fibrils

Treatment: zinc in all cases

Paucibacillary Leprosy: dapsone 1-2 mg/kg to maximum 100 mg self-administered once daily for 6 mo + rifampicin supervised 600 mg orally once a month for 6 mo; follow closely for relapse and restart if necessary

Multibacillary Leprosy: as above + clofazimine supervised 300 mg orally once monthly + 50 mg orally self-administered daily; continue complete regimen for at least 2 y and until negative for organisms; if clofazimine totally unacceptable due to skin discolouration, substitute ethionamide/prothionamide 250-375 mg orally daily self-administered

Prevention and Control: treatment of active cases

BRUCELLOSIS (FEBRIS UNDULANS, MIMIC DISEASE, UNDULANT FEVER): usually a generalised disease but may give rise to numerous localised complications; occasionally, some of these localised conditions may arise independently of systemic disease (eg., pneumonia resulting from inhalation of infected aerosols); these local conditions include bronchitis, pneumonia, meningitis, encephalitis, arthritis, osteomyelitis, osteochondritis, orchitis, cholecystitis and endocarditis; worldwide; transmission by contact with infected animals, ingestion of raw milk, goat cheese made from unpasteurised milk, contaminated meats; natural reservoir in domestic animals such as cattle, goats, sheep and swine; in Australia, cattle herds are free of *Brucella abortus, Brucella canis* and *Brucella melitensis* are not found, and *Brucella suis* is found only in wild pigs; ≈ 50 notified cases/y in Australia (≈ 94% in Queensland); incubation period 1 w to several mo; duration of illness: acute < 60 d, subacute 60 d-1 y, chronic, > 1 y; fatality rate <1% but can cause significant illness for months to years

Agents: *Brucella abortus, Brucella canis, Brucella melitensis, Brucella suis*

Diagnosis: incubation period 5-60 d (usually 1-2 mo); 2/3 of cases chronic or undulating disease with wavelike relapses of weakness, headache, constipation, insomnia, generalised aches and fever; 1/3 of cases acute symptomatic illness with severe malaise in 92%, moderate or high fever (38.3-40°C) in 91-96%, fatigue and weakness in 88%, myalgia in 69%, weight loss in 63%, chills in 40-82%, drenching sweats in 39-99%, osteoarticular complications in 37%, headache (usually severe) in 23-79%, musculoskeletal symptoms (especially tenderness over spine) in 22-66%, arthralgia in 19%, gastrointestinal symptoms (diarrhoea, bloody stools, vomiting during acute phase) in 17-30%, hepatosplenomegaly in 17-47%, cough in 17%, sacroiliitis in 8-15%, pneumonia in 8%, lymphadenopathy in 7-21%, rash in 4%, malodorous perspiration and dysgeusia common; may present with localised symptoms such as ischemic limb, mediastinal mass, dementia; 5% of cases have microscopic hematuria; prostration, delirium, coma and death can occur within days or weeks; in recovering patients, relapses (anorexia, diarrhoea, constipation, colitis in 75%, weight loss, myalgias and arthralgias in 25-50%, bone and joint disease involving weight-bearing and sacroiliac joints in 20-60%, papular, maculopapular, erythema nodosum-like or purpuric eruptions in < 5%, endocarditis (rare but most common cause of death) can occur for weeks and gradually diminish in severity until patient recovers; generalised lymphadenopathy and hepatosplenomegaly; granulomas in liver, spleen, bone marrow, lymph nodes, brain, skin and kidneys; mild leucopoenia, thrombocytopenia

Acute and Subacute: bone marrow culture (positive in 92%), blood cultures (positive in 54-90%), serology, direct immunofluorescence after incubation in nutrient broth; standard tube agglutination (labour intensive; agglutinins to *Brucella abortus* antigen detect all cases due to *Brucella abortus*, as well as 2/3 of infections with *Brucella melitensis* and *Brucella suis*; significant titres (> 160) appear late in second week; cross-reactions occur with *Proteus* OX-19 antigen, *Yersinia, Vibrio, Francisella*; measures IgM mainly but also IgG; becomes low or negative later)

Chronic: 2-mercaptoethanol test (measures IgG), antihuman globulin (Coomb's) test (measures non-agglutinating IgG and some IgA), complement fixation test (measures IgG), ELISA (IgA, IgG, IgM), fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Treatment:

< 8 y: cotrimoxazole 4/20-6/30 mg/kg orally 12 hourly for 6 w + rifampicin 15 mg/kg orally once daily for 6 w (relapse rate 2%) or gentamicin 7.5 mg/kg i.v. daily for 2 w (adjust dose for renal function)

> 8 y: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 6 w (not pregnant or breastfeeding) + rifampicin 15 mg/kg to 600 mg orally once daily for 6 w (relapse rate 8%) or gentamicin (< 10 y: 7.5 mg/kg; child ≥ 10 y: 6 mg/kg; adult: 4-6 mg/kg) i.v. as single daily dose for 2 w (adjust dose for renal function); ciprofloxacin 500 mg orally twice a day + rifampicin 600 mg orally 4 times a day for 30 d

Prophylaxis: live vaccine (veterinary use); pasteurisation of milk products

GLANDERS: an uncommon disease of horses and other equines, on rare occasions transmitted to man; may be acute, affecting mainly the nose, or chronic, causing cutaneous, pulmonary or gastrointestinal nodular lesions

Agent: *Burkholderia mallei*

Diagnosis: incubation period 1-21 d; Gram stain and culture of swab of discharge from necrotic foci in skin or from enlarged regional lymph nodes (also blood, sputum, nasopharyngeal discharge); complement fixation test, agglutinations; contact with horses or mules

Treatment and Prophylaxis: as for **MELIOIDOSIS**

MELIOIDOSIS (PSEUDOCHOLERA, STANTON DISEASE, WHITMORE DISEASE, WHITMORE FEVER): SE Asia and Northern Australia, also Africa, N America; acute septicemic (57% of cases; 45% disseminated, 12% nondisseminated; associated with diabetes mellitus and hematological diseases; often associated with patchy pneumonitis), acute localised and suppurative (42% of cases; cellulitis, subcutaneous abscess, infected wound, septic arthritis of knee, ankle and elbow joints, osteomyelitis, liver abscess, splenic abscess, pyelonephritis, prostatitis or prostatic abscess, lymphadenitis or lymphatic abscess, pericarditis, pericardial effusion common; erythema gangrenosum, hemorrhagic bleb, cutaneous pustules, pyomyositis, urticaria, mastitis, subperiosteal abscess, cholangitis, pancreatic abscess, epididymoorchitis, perinephric abscess, scrotal abscess, endocarditis, endarteritis, meningitis, encephalitis, intracisternal abscess, ophthalmitis (corneal ulcer), parotid abscess rare), acute or chronic pulmonary (pneumonitis, lung abscess, pleural effusion, empyema common; miliary, granuloma rare; chronic resembles tuberculosis and is marked by granulomatous abscess formation), chronic suppurative (chronic granuloma)

Agent: *Burkholderia pseudomallei*

Diagnosis: incubation period 1-21 d; manifestations vary from asymptomatic to rapidly overwhelming septicemia (case-fatality rate 85-95%), prolonged fever without localising signs, localised infections (either acutely suppurative or chronic and granulomatous), septicemia of abrupt onset with metastatic lesions in skin, muscle, bone and joints; culture of pus swab from ulcers and abscesses, sputum, urine, blood; indirect hemagglutination antibody titre (< 1:80, unlikely; 1:80-1:320, suggestive; > 1:320, very likely)

Treatment: ceftazidime 50 mg/kg to 2 g i.v. 6 hourly or meropenem 25 mg/kg to 1 g i.v. 8 hourly or imipenem 25 mg/kg to 1 g i.v. 6 hourly for at least 14 d (4-8 w in deep-seated infections, osteomyelitis, septic arthritis), then cotrimoxazole 8 + 40 mg/kg to 320 + 1600 mg orally 12 hourly + folic acid 0.1 mg/kg to 5 mg orally daily ± doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not < 8 y) for at least further 3 mo

Prophylaxis (Postexposure): cotrimoxazole 8 + 40 mg/kg to 320 + 1600 mg orally 12 hourly, doxycycline 100 mg orally 12 hourly (adults only)

NON-PNEUMONIC LEGIONNAIRE'S DISEASE (FORM CHARACTERISED BY MALAISE, MYALGIA AND HEADACHE KNOWN AS PONTIAC FEVER): a self-limited febrile disease

Agents: species of genera *Fluoribacter, Legionella* and *Tatlockia*

Diagnosis: malaise, myalgia, headache, encephalopathy (and possibly other neurological syndromes) and gastrointestinal upset, mainly diarrhoea; serology

Treatment: erythromycin

PLAGUE (BLACK DEATH, GREAT MORTALITY, ORIENTAL PLAGUE, PEST, PESTIS): ≈ 1800 cases/y (240 deaths) worldwide; great deal of central and eastern Africa—Tanzania ≈ 900 cases (70 deaths), Zaire ≈ 320 cases (85 deaths)/y, Madagascar ≈ 260 cases (60 deaths)/y, Asia total ≈ 960 cases (50 deaths)/y, Vietnam ≈ 600 cases (25 deaths)/y, Burma ≈ 280 cases (4 deaths)/y, recent outbreak in India, Americas total ≈ 520 cases (30 deaths)/y, Western USA, ≈ 40 cases (7 deaths)/y, Peru ≈ 260 cases (20 deaths)/y; last notification in Australia in 1923; killed 40% of population of Constaninople in 541 and 542, 44 M in Europe in latter half of fourteenth century, 12 M in India 1896-1936; bubonic plague (glandular plague, malignant polyadenitis, pestis bubonica, pestis fulminans, pestis major, polyadenitis maligna, St Roch disease, Tarabagan disease; most frequent form; characterised by inflammation and enlargement of lymphatic glands, especially in groin (pestis inguinaria) and axilla; hemorrhage may occur (black plague, hemorrhagic plague); cervical form associated with meningitis and pneumonia; mortality in untreated 50-60%), primary pneumonic plague (pulmonary plague; arises from inhalation, usually rapidly fatal; secondary plague pneumonia is complication of plague elsewhere in body through hematogenous spread, variable in severity), pharyngeal plague (anginal plague, tonsillar plague; result of exposure to larger infectious droplets or ingestion of infected tissues), septicemic plague (pesticemia, pestis siderans; primary septicemic

plague; relatively infrequent, no involvement of lymphatics and no buboes); bubosepticamic plague (secondary septicemic plague; more frequent, result of delay in treatment of bubonic plague); transmission by infected rodents and fleas (*Xenopsylla cheopis*), pus from lesions, sputum; zootic plague resulting from transmission from an animal; may be sylvatic (rodents living in wooded areas), campestral (rodents living in plains) or domestic (peridomestic, agrestial; in 'domestic' rodents and domestic cats), demic (mostly from transmission from other humans)

Agent: *Yersinia pestis*

Diagnosis: incubation period 1-6 d; prostration in 75% of cases, chills in 40-61%, headache in 40-55%, abdominal pain in 39% of septicemic and 8% of bubonic, malaise in 38-44%, vomiting in 33-50%, confusion in 30%, nausea in 29-44%, cough in 25%, diarrhoea in 23-39%, chest pain in 15%, fever, lymphadenitis (bubo), meningitis; geographic history; contact with rodents; Gram stain, fluorescent antibody stain and culture of lymph node and bubo aspirates, sputum; blood cultures; also sputum, CSF and urine; identify isolates by fluorescent antibody and bacteriophage; fourfold or greater change in serum antibody titre to *Yersinia pestis* F1 antigen (serum passive hemagglutination; ELISA (sensitivity 100%)); rapid monoclonal antibody test (sensitivity 100%, specificity 100%, positive predictive value 91%, negative predictive value 87%) white cell count 9000-17,400/μL with marked shift to left, 79% neutrophils, 13% bands, 5% monocytes, 3% lymphocytes; gross haematuria, 4+ proteinuria, many granular and red blood cell casts, pyuria, bacteriuria

Treatment: gentamicin 4-7.5 mg/kg/d i.v., doxycycline 4 mg/kg to 200 mg i.v. then 2 mg/kg to 100 mg i.v. twice daily (not < 8 y), ciprofloxacin 15 mg/kg to 400 mg i.v. twice daily, chloramphenicol 25 mg/kg i.v. 4 times a day

Prophylaxis (Postexposure): doxycycline 2 mg/kg to 100 mg orally 12 hourly (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly

Pseudotuberculosis (Rodent Pseudotuberculosis): 3 forms: systemic pseudotuberculosis, pseudotuberculous enterocolitis, pseudotuberculous mesenteric lymphadenitis

Agent: *Yersinia pseudotuberculosis*

Diagnosis: culture of appropriate specimen

Treatment: gentamicin, cefotaxime, doxycycline, ciprofloxacin

Tularemia (Alkali Disease, Deer-Fly Disease, Francis Disease, Ohara Disease, Pahvant Valley Fever, Pahvant Valley Plague, Rabbit Fever, Yato-bigo, Yato-byo): Europe, Japan, USA, former Soviet Union; incidence 0.1/100,000 in USA; 75-85% ulceroglandular (fever, development of a cutaneous ulcer at the site of infection, with regional, and sometimes general, lymphadenopathy), 5-15% typhoidal (generalised tularemia; severe systemic form with septicemia, arising by dissemination via bloodstream from a primary lesion; fever, prostration, weight loss), 1-2% oculoglandular (ophthalmic tularemia; portal of entry is the eye; fever, regional lymphadenopathy, purulent conjunctivitis, swollen eyelids), < 1% oropharyngeal (fever, adenopathy, inflammation of the mouth or pharynx, sometimes resembling tonsillitis), tracheobroncitis (primary from inhalation of contaminated material or secondary from dissemination via bloodstream), bronchopneumonia and lobar pneumonia, gastrointestinal (abdominal tularemia, ingestion tularemia; gastrointestinal lesions, often severe); death in 18%; transmission by contact with infected animal (eg., rabbit), ticks (*Dermacentor variabilis* and *Ambylomma americanum* in southern and eastern USA, *Dermacentor andersoni* in southern and western USA), deerfly, rarely cat bite

Agent: *Francisella tularensis*

Diagnosis: residence in, or visit to, endemic area; exposure to ticks, rabbits or other animals; incubation period 1-57 d (average 4 d); fever in all, cutaneous ulcer in 64%, painful adenopathy in 55%, cough in 45%, diarrhoea in 18%, headache, malaise, pneumonia, pleural effusion and patchy infiltrates on chest X-ray; culture of nodules, pustules, ulcers, lymph node aspirate, blood, pleural exudate or sputum on glucose-cysteine agar; fluorescent antigen staining of exudates; microagglutination, tube agglutination, ELISA (sensitivity 96%, specificity 98%); animal inoculation; erythrocyte sedimentation rate 40 mm/h; white cell count 11,400/μL, 60% segmented neutrophils, 16% band forms, 13% lymphocytes, 2% atypical lymphocytes, 5% monocytes

Treatment: gentamicin 4-7.5 mg/kg i.v. daily for 10 d, doxycycline (< 45 kg, 2.2 mg/kg i.v. twice daily for 14-21 d; $\geq$ 45 kg, 100 mg i.v. twice a day), chloramphenicol 15 mg/kg i.v. 4 times a day for 14-21 d, ciprofloxacin 15 mg/kg i.v. twice a day for 10 d

Prophylaxis (Postexposure): doxycycline 2.5 mg/kg to 100 mg orally 12 hourly (not < 8 y), ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly

Prevention and Control: avoid contact; regularly detick dogs with 6% malathion powder

Rat Bite Fever: usually transmitted by bite of rats and certain other animals but, in the case of streptobacillosis, transmission via contaminated milk has occurred and the disease has been reported in the absence of bites following contact with live or dead rats or dogs

Agents: *Streptobacillus moniliformis* (epidemic arthritis erythema, Haverhill fever, streptobacillary fever; distinctly uncommon disease of N and S America; single case reported from Australia; complications uncommon but severe; case-fatality rate $\approx$ 13%), '*Spirillum minus*' (Sodoka; complications very rare; case-fatality rate $\approx$ 6%)

Diagnosis: dark ground, Gram stain, culture and guinea pig inoculation of pus from bite site, metastatic abscess or infected joint, lymph gland aspirate, blood; serology; marked neutrophilia

'***Spirillum minus***': Gram negative, spiral; incubation period > 10 d; local skin reaction at site of bite; regional lymphadenopathy; chills; arthritis and leucocytosis rare; isolation of organism by animal inoculation; no specific serology; false positive serologic test for syphilis in > 50% of cases

Streptobacillus moniliformis: microaerophilic, Gram negative, pleomorphic; incubation period < 10 d; no local skin reaction at site of bite; lymphadenopathy and chills rare; polyarthritis and leucocytosis present; palmar and plantar rash; isolation of organism in artificial medium; serology; false positive test for syphilis in < 25% of cases

Treatment: aqueous procaine penicillin 600,000 U i.m. twice daily (child: 25,000-50,000 U/kg daily in 2 divided doses) for 7-10 d; phenoxymethylpenicillin 500 mg orally 6 hourly (< 12 y: 25-50 mg/kg orally daily in 4 divided doses) for 7-10 d, tetracycline 500 mg orally 6 hourly for 7-10 d, erythromycin 500 mg orally 6 hourly (child: 30-50 mg/kg daily in 4 divided doses) for 7-10 d

Differential Diagnosis: acute viral exanthems, rickettsial infections, drug reactions, septic arthritis, leptospirosis, collagen-vascular diseases, secondary syphilis, neisserial infections, influenza, infective endocarditis, acute rheumatic fever, malaria, relapsing fever, lymphoma/leukemia

Disseminated Gonococcal Disease: a generalised gonococcal disease arising as a result of hematogenous spread, usually from a urogenital tract or pharyngeal disease; during septicemic phase, manifested by cutaneous (especially palmar and plantar) lesions that develop necrotic centres (gonococcal keratosis, gonococcal dermatitis, gonococcal dermatosis, keratoderma blenorrhagica, keratosis blennorrhagia); occurs most frequently in women; may be manifested by any of numerous clinical conditions, including gonococcal endocarditis, gonococcal myocarditis, gonococcal pericarditis, gonococcal meningitis, gonococcal brain abscess, gonococcal peritonitis and gonococcal pneumonia; frequently gives rise to arthritis and occasionally to septicemic adrenal hemorrhage syndrome

Agent: *Neisseria gonorrhoeae*

Diagnosis: blood cultures; culture of other specimens as appropriate

Treatment: benzylpenicillin 10 MU i.v. daily until patient improves, followed by 500 mg 6 hourly to complete at least 7 d of treatment; amoxycillin 3 g orally once as a single dose + probenecid 1 g orally once as a single dose, followed by amoxycillin 500 mg orally 6 hourly for at least 7 d; ceftriaxone 1 g i.v. daily for 7 days; tetracycline 500 mg orally 6 hourly for at least 7 d; cefoxitin 1 g i.v. 6 hourly for at least 7 d; cefotaxime 500 mg i.v. 6 hourly for at least 7 d; erythromycin 500 mg orally 6 hourly for a minimum of 7 d; ceftriaxone 1 g for 24 - 48 h, then ciprofloxacin for 7 d

Disseminated Meningococcal Disease: generalised disease arising as a result of hematogenous spread of *Neisseria meningitidis*, manifested by severe toxemia and intravascular coagulation, usually with hemorrhagic signs varying from small petechiae to widespread extravasation of blood; meningitis usually absent; occasionally gives rise to numerous clinical conditions, including meningococcal carditis, meningococcal endocarditis, meningococcal myocarditis, meningococcal pericarditis, meningococcal arthritis and meningococcal conjunctivitis; most common cause of septicemic adrenal hemorrhage syndrome

Agent: *Neisseria meningitidis*

Diagnosis: incubation period < 21 d; blood cultures

Treatment: as for **Disseminated Gonococcal Disease;** activated protein C

Prophylaxis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

Rickettsioses: cause 2% of fever in returned travellers to Australia

Agents: *Rickettsia rickettsii* (spotted fever, American spotted fever, black fever, Brazilian spotted fever, Bullis fever, Choix fever, Colombian tick fever, eastern-type Rocky Mountain spotted fever, exanthematous typhus of Sao Paulo, Lone Star fever, Mexican spotted fever, New World spotted fever, pinta fever, Rocky Mountain spotted fever, Sao Paulo fever, Sao Paulo typhus, Texas tick fever, Tobia fever (Colombia), western-type Rocky Mountain spotted fever; Western Hemisphere; 3 cases/million in USA (23/million in North Carolina); wood tick (*Dermacentor andersoni*) vector in northeastern USA, dog tick (*Dermacentor variabilis*) in eastern and southern USA, and 'Lone Star' tick (*Amblyoma americana*) in southeastern USA; vertebrate host rodents, dogs, rabbits, opossum), *Rickettsia conorii* (spotted fever, African tick fever, Boutonneuse fever, Conor and Bruch disease, eruptive Mediterranean fever, fièvre boutonneuse, India tick typhus, Kenya tick typhus, Marseilles fever, Mediterranean exanthematous fever, Mediterranean tick fever, Olner disease, South African tick bite fever; Mediterranean, Black Sea and Caspian Sea littorals, Middle East, India, Africa; tick (*Rhicephalus sanguineus*) vector; vertebrate host rodents, dogs), *Rickettsia akari* (rickettsialpox, Kew Garden fever, Kew Garden spotted fever, vesicular rickettsialpox; N America, former Soviet Union, Southern Africa, Korea, Mediterranean; mites vector; vertebrate host mice, rat), *Rickettsia sibirica* (spotted fever, North Asian tick fever, Siberian tick typhus; Armenia, Central Asia, Siberia, Mongolia, Central Europe; tick vector; vertebrate host rodents), *Rickettsia australis* (North Queensland tick typhus, Queensland coastal

fever, Queensland fever, Queensland tick typhus; eastern coast of Australia east of the Great Dividing Range; tick (*Ixodes holocyclus*) vector; vertebrate host marsupials), *Rickettsia honei* (Flinders Island spotted fever; Flinders Island (Bass Strait) and Schuten Island (east coast of Tasmania); *Aponomma hydrosauri* (reptile tick) vector), '*Rickettsia pijperi*' (tick bite fever; S Africa), *Rickettsia prowazekii* (typhus fever (blasting typhus, camp fever, classical endemic typhus, classic typhus, epidemic typhus, European typhus, exanthematous typhus, famine fever, Fleckfieber, flecktyphus, gaol fever, Hildebrand disease, hospital fever, jail fever, louse-borne typhus, louse typhus, primary epidemic typhus, ship fever, typhus, typhus exanthematicus, war fever) and benign typhus (Brill disease, Brill-Zinsser disease, recrudescence fever, recrudescent fever, recrudescent louse-borne typhus, recrudescent typhus, sporadic typhus, typhus sidera) for form appearing years after complete recovery; human body louse (*Pediculus humanus corporis*) vector; vertebrate host man, squirrels; epidemic disease, late recrudescence; 'sylvatic typhus' in eastern USA probably transmitted by squirrel fleas; not seen in Australia since gold rush and convict times), *Rickettsia typhi* (typhus fever, benign typhus, Congolian red fever, endemic typhus, fièvre nautique, flea-borne tarbardillo, flea-borne typhus, latent typhus, Manchurian fever, Manchurian typhus, Mexican typhus, Moscow typhus, murine typhus fever, rat-borne typhus, rat typhus, red fever of the Congo, ship typhus, shop typhus (Malaysia), Toulon typhus, typhus marinus, urban tropical typhus; worldwide, with outbreaks reported from Australia, China, Greece, Israel, Kuwait, Thailand; < 100 cases/y in USA; vector flea (classically, rat flea *Xanopsylla cheopsis,* but free-ranging cats, dogs, opossums and their fleas assuming increasing importance) and rat louse; vertebrate host wild rats, field mice), *Rickettsia africae* (African tick bite fever; main cause of rickettsiosis in travellers to sub-Saharan Africa; transmitted by *Ambylomma* tick), *Orientia tsutsugamushi* (typhus fever, akamushi disease, akamushi fever, Burma eruptive fever, chigger-borne rickettsiosis, China fever, flood fever, inundation fever, island disease, island fever, island typhus, Japanese flood fever, Japanese river fever, kedani disease, kedani fever, Malayan fever, mite-borne typhus, mite typhus, rural typhus, scrub fever, scrub typhus, shashitsu, shima-mushi disease, shimu-mushi, Shishito, Sumatran typhus, tsutsugamushi, tsutsugamushi disease, tsutsugamushi fever, yochubyo; Asia, Indian subcontinent, tropical northern Australia, Pacific Islands, Indonesia; trombiculid mites (*Leptotrombidium deliense* in Australia) vector; vertebrate host native rodents, bandicoots), *Rickettsia sibirica* (Siberian tick typhus; central Asia; tick vector; rodents, dog reservoir), *Coxiella burnetii* (Q fever, Australian Q fever, Australian typhus, Balkan grippe, Derrick-Burnet disease, Nine Mile fever, quadrilateral fever; worldwide; vector tick (unnecessary); vertebrate host sheep, cattle, goats; respiratory pathogen, infection by aerosol from vertebrate carrier; ≈ 700 notified cases/y in Australia (≈ 40% in Queensland)), *Ehrlichia sennetsu* (Hyuga fever), *Rickettsia felis* (transmitted by cat fleas; causes murine typhus-like syndrome); **EHRLICHIOSIS** see Chapter 10.

Diagnosis: incubation period 7-14 d; acute onset, fever, true rigours, rash (except in Q fever; macular, maculopapular or petechial, starting on extremities and extending to trunk, with regular occurrence on palms and soles in Rocky Mountain spotted fever; vesicular or vesiculopapular (may be sparse or diffuse) in rickettsialpox; macular or maculopapular, starting on trunk and extending to extremities in typhus fever), headache, arthralgias, myalgias, conjunctivitis; primary lesion in Boutonneuse fever, Siberian tick typhus, Queensland tick fever, scrub typhus; adenopathy in scrub typhus; murine typhus mild disease; tachypnoea in 97% of cases of typhus fever, fever in 85%, conjunctival suffusion in 53%, raised erythrocyte sedimentation rate in 57%, increased lactate dehydrogenase in 82%, aspartate aminotransferase increased in 63%, severe involvement of CNS, myocardium and kidneys not unusual; spotted fever due to *Rickettsia sibirica* resembles that due to *Rickettsia rickettsii* but is less severe; usually leucopenia with rickettsialpox; often pneumonitis in tsutsugamushi (relapses and second attacks common); on rare occasions, Q fever may become latent and reappear as chronic condition, usually complicated by chronic hepatitis, thrombocytopenia and endocarditis (latter invariably fatal if untreated); manifestations of *Ehrlichia sennetsu* infection vary from low grade fever with mild headache and slight back pain to persistent high fever, anorexia, lethargy, lymphadenopathy and prominent hematological abnormalities; geographic, epidemiological; indirect microimmunofluorescence; ELISA (antibody); growth in tissue culture (VERO or L929); Weil-Felix (Boutonneuse fever, Rocky Mountain spotted fever, tick bite fever, tick typhus: OX19^{+}, OX2^{+}, tenth to fourteenth day; epidemic typhus, murine typhus: OX19^{+}, OX2$^{\pm}$; scrub typhus: OXK^{+}; Brill's disease: usually negative; Q fever, rickettsialpox: negative; specificity not absolute; many false positive and false negative reactions occur; cross-reactions with typhoid, *Proteus* urinary tract infection, leptospirosis, severe liver disease), complement fixation test (tenth to fourteenth day), microscopic agglutination; animal inoculation; lysis-centrifugation blood cultures

Boutonneuse Fever: microimmunofluoresecence, latex agglutination of serum; immunofluorescence of skin lesion biopsy; Western blot; isolation of *Rickettsia conorii* from blood culture with shell vial cell culture; abnormal serum γ-glutamyl transferase in 60% of cases, abnormal SGOT in 55%, abnormal SGPT in 54%

Q Fever: incubation period < 21 d; farm worker, slaughtering or dressing animals, exposure to parturient cats; histology of liver (multiple non-caseating granulomas); complement fixation test (phase 1 negative in first 3-4 w, phase 2 ≥ 4X increased in acute; phases 1 and 2 titre ≥ 160 in chronic), immunofluorescent antibody and ELISA tests (IgG significantly increased in acute, titre ≥ 1280 in chronic; IgA titre ≥ 1280 in chronic; IgM positive in acute, negative or low in chronic)

Rocky Mountain Spotted Fever: incubation period 2 w; fever, spotted rash, headache, myalgia, abdominal pain; pulmonary complication (pharyngitis, pleural effusion, pleurisy; pleural effusion, diffuse infiltrates and pulmonary edema on chest X-ray) occurs; IgM, IgG, serology

'Rickettsia africae': 95% inoculation eschar (54% multiple), 88% fever, 63% influenza-like syndrome, 63% myalgias, 46% rash (usually maculopapular or vesicular, rarely purpuric), 43% regional lymphadenopathy; microimmunofluorescence assay + Western blot + cross-adsorption assay (sensitivity 56%; each test positive predictive value and specificity 100%)

Treatment:

Q Fever:

Acute: doxycycline 2 mg/kg to 100 mg orally 12 hourly for 14 d (not < 8 y, pregnant or breastfeeding), chloramphenicol 12.5 mg/kg to 500 mg i.v. 6 hourly for 14 d

Chronic: doxycycline or chloramphenicol + rifampicin or hydroxychloroquine for 2 y

Endocarditis: see **ENDOCARDITIS**

Australian Spotted Fever, Tick Typhus, Scrub Typhus, Rocky Mountain Spotted Fever, Epidemic Typhus, Endemic Typhus: doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 7-10 d (not < 8 y), chloramphenicol 12.5 mg/kg to 500 mg i.v. 6 hourly for 7-10 d (until afebrile for 2-3 d)

Others: tetracycline or doxycycline as above

Prophylaxis: doxycycline 200 mg orally weekly; use of protective clothing and tick repellent containing N,N-diethyl-m-toluamide in tick areas

Rocky Mountain Spotted Fever: incomplete natural immunity; vaccine available (yearly booster, exposed persons)

Rickettsialpox: complete natural immunity; no vaccine available

Epidemic Typhus: natural immunity gives complete protection against infection but recrudescent illness in some individuals common; vaccine available (epidemics)

Endemic Typhus: natural immunity gives protection against both endemic and epidemic typhus; vaccine available but not recommended

Scrub Typhus: natural immunity gives complete protection for strain of organism but second infection with another strain occurs; no vaccine available

Q Fever: complete natural immunity; vaccine available for laboratory workers, animal processors

TRENCH FEVER (FEBRIS QUINTANA, 5-DAY FEVER, HIS-WERNER DISEASE, IKAWA FEVER, MEUSE FEVER, QUINTAN FEVER, SALONICA FEVER, SALONIKI FEVER, SHANK FEVER, SHIN-BONE FEVER, TIBIALGIC FEVER, VAN DER SHEER FEVER, VOLHYNIA FEVER, WERNER-HIS DISEASE, WOLHYNIAN FEVER): Europe, Africa, S and Central America, Russia; louse vector; vertebrate host man; extracellular growth

Agent: *Bartonella quintana*

Diagnosis: primary inoculation site, discrete macular rash, sweating and splenomegaly common; serology; smear and culture; PCR

Treatment: erythromycin, doxycycline, tetracycline, minocycline, rifampicin, ciprofloxacin

Prophylaxis: doxycycline 200 mg orally weekly; use of protective clothing and tick repellent containing N,N-diethyl-m-toluamide in tick areas; incomplete natural immunity; no vaccine available

YAWS (BOBA, BOUBI, BREDA DISEASE, BUBA, CHARLOUIS DISEASE, COKO (FIJI), DUBE, FRAMBOESIA TROPICA, PARANGI (SRI LANKA), PURRU (MALAYSIA), TONGA, TROPICAL YAWS): acute and chronic; transmission by indirect or direct nonvenereal contact

Agent: *Treponema pallidum subsp pertenue*

Diagnosis: preclinical incubation period of 3-5 w; initial yaws (initial framboesia, primary framboesia, primary yaws) begins as a papule and becomes either papillomatous (chancre of yaws, chancre pianique, mother yaw, primary framboesioma) or ulceropapillomatous (initial framboesial ulcer, ulcère post-chancreux); cutaneous involvement in early yaws is manifested by a wide variety of lesions—plaques (yaws patches), erythematous macular yaws (erythematous macular framboesia, roséle pianique), squamous macular early yaws (depigmented framboeside, furfuraceous macular framboeside, yaws trash), macular early yaws, papillomatous early yaws (butter yaws, framboesia secundaria papillomatosa, framboesioma, pianoma, papilloma tropicum, tropical papilloma; includes palmar and plantar papillomatous early yaws (crab yaws, framboesia papillomatous palmaris/plantaris, pian guigne, wet crabs, web crab yaws)), palmar and plantar squamous macular early yaws (erythematous squamous psoratiform plaque of yaws, papulosquamous palmar/plantar pianides, squamous plaques of yaws, yaws of the first type of Baerman), palmar and plantar hyperkeratotic macular early yaws (hyperkeratosis and trichophytoid pianides, keratomas of yaws, keratoderma punctata of yaws, polymorphic hyperkeratosis of yaws, punctate keratosis of palms/soles, worm-eaten soles), squamous maculopapular early yaws (lichenoid pianide, pityriasiform pianide), simple papular early yaws, umbilicate papular early yaws (hyperkeratotic papules), acuminate micropapular early yaws (follicular framboeside, folliculopapular framboeside; desquamation may case apparent depigmentation), squamous micropapular

early yaws (corymbiform framboeside, furfuraceous framboeside, keratitis-pilaris-like framboeside, lichenoid macular framboeside, papulosquamous framboeside, pityriasiform framboeside, pain dartre); mucosal early yaws may be either maculopapular or papillomatous; osteoarthropathy (osteitis, periostitis, osteoperiostitis (frequently polydactylitis (spina ventosa pianides)), osteomyelitis, hydrarthrosis (synovitis), ganglion) in early yaws is usually nondestructive and most frequently affects shafts of long bones; latent yaws with no symptoms; late yaws characterised by destructive lesions of skin—plaques (papulo-erythematous framboeside; squamous, well demarcated lesions), nodular late yaws (gummatous framboesides, gomme pianique; cutaneous or subcutaneous nodular lesions), ulcerated nodular late yaws (tuberculo-crusted circinate ulcers of yaws, yaws ulcers; ulcerated nodular lesions which may result in keloid scarring, contractures and pigmentary changes), palmar and plantar hyperkeratotic late yaws (ghoul hand, keratosis palmaris/plantaris of yaws, pintoid lesions of yaws, yaws hyperkeratosis with trichophytoid characteristics, yaws keratodermia; polymorphic, ill-defined hyperkeratotic lesions of palms or soles, with tendency to leave scars and pigmentary changes (leukomelanoderma)), mucous membrane and bone—osteitis, periostitis, osteoperiostitis, arthritis, hydrarthrosis (synovitis), ganglion, juxta-articular nodules of late yaws (Lutz-Jeanselme nodules; fibromatous tumour like masses arising beneath skin in vicinity of joints), goundou (hyperkeratotic osteitis of nasal processes of maxilla, frequent in Africa, not seen in some areas), gangosa (ogo, rhinopharyngitis mutilans; ulcerative destructive lesion of nose and hard palate which may cause severe disfiguration); serology

Treatment: penicillin

LEPTOSPIROSIS (AKIYAMI B, AUTUMNAL FEVER, AUTUMN FEVER, CANE-CUTTER'S DISEASE, CANE-FIELD FEVER, FELDFIEBER B, FIELD FEVER, HASAMI FEVER, JAPANESE SEVEN-DAY FEVER, LEPTOSPIROSIS FEBRILIS, MUD FEVER, NANUKAYAMI, PEA-PICKER'S DISEASE, SCHLAMMFIEBER, SLIME FEVER, SPIROCHAETASIS, SWAMP FEVER, SWINEHERD'S FEVER, WATER FEVER): ≈ 300 notified cases/y in Australia (≈ 70% in Queensland; incidence 1.9/100,000; 11% prevalence in banana growers); wherever domestic animals are kept, particularly pigs; survival enhanced by alkaline pH of animal urine, ground water and soil (days to weeks under optimal conditions); concentrated in summer and early autumn; most cases during childhood through middle age because of increased hazards resulting from recreational and occupational activities; transmission by food or water contaminated with animal (eg., rat) urine; incubation period 4-19 d

Agent: *Leptospira interrogans*

Diagnosis: incubation period < 21 d; asymptomatic to severe (with jaundice, anemia, hemorrhage and renal failure; epidemic spirochaetal jaundice, hemorrhagic jaundice, icterogenic spirochaetosis, icterohemorrhagic jaundice, Indonesian Weil disease, infectious spirochaetal jaundice, Landouzy disease, leptospiral hemorrhagic icterus, leptospiral jaundice, leptospirosis icterohemorrhagica, Mathieu disease, ricefield fever, spirochaetosis icterohemorrhagica, spirohematosis icterohemorrhagica, Vasilev disease, Weil icterus, Weil syndrome); typically a biphasic disease, the first phase being an acute febrile illness with leptospiremia and a wide variety of manifestations and the second (urine) phase being less febrile with different manifestations; fever in 75-90% of cases, headache in 66%, severe myalgias in 40-55% (pain on raising extended leg positive predictive value of 67%), stiff neck in 40%, arthralgia in 38%, CSF pleocytosis in 35%, jaundice in 35%, CSF protein increased in 30%, nausea and/or vomiting in 30%, rigours in 19%, rash in 15%, chills in 10%, conjunctivitis or conjunctival hemorrhage in 9%; pulmonary hemorrhage may occur; sudden onset; phase examination and culture of blood (first week of infection), urine (second and third weeks of infection); serology (complement fixation test detects antibodies to group antigen, 4-fold rise in titre diagnostic, titres > 160 in abattoir workers and veterinarians, negative result does not exclude infection; microscopic agglutination test distinguishes antibody to range of serovars; ELISA sensitivity 100%, specificity 93-100%; Lepto dri-dot test for IgM gives comparable results to ELISA and is faster, more economical and does not require sophisticated equipment or skilled personnel); culture and inoculation of young hamster or guinea-pig with CSF or blood; normochromic anemia with marked neutrophilia; raised erythrocyte sedimentation rate; hematuria in 25%, protein ± casts in urine in 20%, oliguria in 15%; history of exposure to animals (30% dogs, 10% cattle/swine, 8% rodent, 5% wildlife (skunks, raccoons, foxes, opossums, armadillos; horses), occupational (construction, farm, veterinary, abattoir) or recreational (swimming in contaminated water, hunting) exposure (incubation period usually 7-14 d)

Serovar canicola: influenza-like illness followed by meningitis

Serovar hardjo: usually a less severe disease with influenza-like symptoms, slight meningitis, slight renal failure

Serovar icterohaemorrhagiae: jaundice, renal failure, meningitis

Differential Diagnosis: meningitis (initial diagnosis in 30% of cases), hepatitis (initial diagnosis in 15%), encephalitis (initial diagnosis in 10%), fever of unknown origin (initial diagnosis in 9%), pneumonia (initial diagnosis in 2%), influenza (initial diagnosis in 2%)

Treatment: administer within first 4 d of illness; doxycycline 2.5 mg/kg to 100 mg orally 12 hourly for 5-7 d (not < 8 y, pregnant or breastfeeding), benzylpenicillin 30 mg/kg to 1.2 g i.v. 6 hourly for 5-7 d, ceftriaxone 25 mg/kg to 1 g i.v. daily for 5-7 d, cefotaxime 25 mg/kg to 1 g 6 hourly for 5-7 d

Prevention and Control: good sanitation

Relapsing Fever (Bilious Typhoid Fever, Febris Recurrentis, Polyleptic Fever, Recurrent Fever, Spirillum Fever, Typhus Recurrens): general term for a systemic borreliosis in man, characterised by alternating febrile and nonfebrile periods, each of the febrile periods ending in crisis

Agents: louse-borne: *Borrelia recurrentis* (carapata, carapata disease, epidemic relapsing fever, European relapsing fever, famine fever, louse-borne relapsing fever, Obermeier relapsing fever, vagabond fever); tick-borne: *Borrelia crocidurae, Borrelia duttonii* (D fever, Dutton fever, Dutton relapsing fever, Novy relapsing fever), *Borrelia hermsii, Borrelia hispanica, Borrelia parkeri, Borrelia persica* (miameh disease, miameh relapsing fever, miana disease), *Borrelia turicatae*, several other species

Diagnosis: disease usually begins with rigours and fever, nausea, vomiting, photophobia, arthralgia and myalgia, followed by marked pulmonary signs, hepatosplenomegaly, jaundice and hemorrhagic diathesis; organisms seen in Giemsa or Wright-stained peripheral blood smears or in dark ground microscopy of blood at time of rising temperature in 70% of cases; urinalysis normal to trace of protein, red blood cells, casts; hematocrit 40%, hemoglobin decreased, white cell count 10,000/μL, 71% neutrophils (6% bands), 22% lymphocytes, 8% monocytes; ESR 67 mm/h; serum creatinine and alkaline phosphatase normal, serum bilirubin 3.1 mg/dL, SGOT 55 U/mL, SGPT 67 U/mL; CSF protein 95 mg/dL, glucose 75 mg/dL, 950 cells/μL, organism seen in 10%; Weil-Felix: OX-19 negative, OX-2 negative, OX-K $\geq$ 1:40 in 90% of louse-borne and 30% of tick-borne; complement fixation test for *Borrelia* positive in 50%; positive animal inoculation in 85% of cases

Louse-borne: splenomegaly in 75% of cases, hepatomegaly in 66%, jaundice in 35%, respiratory symptoms in 35%, CNS involvement in 30%, rash in 9%

Tick-borne: splenomegaly in 40%, rash in 25%, hepatomegaly in 15%, respiratory symptoms in 15%, CNS involvement in 9%, jaundice in 7%

Differential Diagnosis: malaria and dengue (febrile periods shorter), leptospirosis (conjunctival suffusion), rat-bite fever (bite history, inflammatory reaction at site of bite), Rocky Mountain spotted fever (rash typically different—first on limbs, involves palms and soles)

Treatment:

Louse-borne: aqueous procaine penicillin 600,000 U (child: 25,000-50,000 U/kg) i.m. at once and repeated after 12-24 h, tetracycline 500 mg orally as a single dose, erythromycin 500 mg orally as a single dose (infants and young children: 25-50 mg/kg daily in divided doses for 4-5 d), chloramphenicol 500 mg orally 6 hourly for 5 d (child > 2 w: 50 mg/kg daily orally in 4 divided doses; premature, newborn and those with immature metabolism: 25 mg/kg daily in 4 divided doses), doxycycline

Tick-borne: tetracycline 500 mg orally 6 hourly for 5-10 d, doxycycline 100 mg orally 12 hourly for 5-10 d Treatment may be complicated by a severe Herxheimer reaction.

Prophylaxis (Within 48 h of Tick Bite): tetracycline 1 g/d for 3-5 d

Prevention and Control: lice and tick control

Lyme Disease (Lyme Arthritis): multi-system, immune-mediated, inflammatory disorder that may last several years; erythema chronicum migrans (exanthema; in 26%), followed (in 10%) by disease of central and peripheral nervous system (aseptic meningitis, encephalitis, cranial and spinal neuropathies, especially unilateral or bilateral Bell's palsy, Garin-Bujadoux-Bunwarti syndrome of meningoencephalitis, cranial neuritis and radiculoneuritis) and (in 6-8%) of heart (atrioventricular conduction defects, myocarditis, pericarditis), by acromodermatitis chronica atrophicans and by solitary or diffuse lymphadenosis benigna cutis, followed (in 50%) by arthritis; hepatitis, nephritis, uveitis, myositis, pulmonary complication (cough, acute respiratory distress, respiratory failure) also occur; recorded from Algeria, Belgium, England, Federal Republic of Germany, France, Italy, Northern Ireland, Scotland, Sweden, USA (95% of vector borne illness; $\approx$ 16,000 cases/y), few cases in Australia; vector *Ixodes ricinus* in Europe, *Ixodes scapularis* in NE, E and midwest USA and *Ixodes pacificus* in western USA, also *Amblyoma americana* and *Dermacentor variabilis,* ? *Ixodes holocyclus* in Australia; principal mammalian host deer; 24-53% of healthy dogs from enzootic areas show serological evidence of infection; ticks acquire infection from rodents (white-footed mice and eastern chipmunks); transplancental transmission documented in child with congenital heart defect; incubation period 1 w stage 1, 5-6 w stage 2

Agent: *Borrelia burgdorferi* group (*Borrelia afzellii* associated with erythema migrans and acrodermatitis chronica atrophicans, *Borrelia burgdorferi* and genospecies *Borrelia garinii* associated with extracutaneous symptoms)

Diagnosis: single erythema migrans 3-30 d after tick bite, with myalgia, arthralgia, fever, headache, fatigue, regional lymphadenopathy; at 1-12 w after tick bite, erythema migrans may become multiple, with neck pain, meningitis, cranial neuritis (facial palsy), radiculoneuritis, carditis (variable hearth block), eye involvement; arthritis and/or chronic CNS involvement may develop after $\approx$ 2 mo; may have pulmonary edema, cardiomegaly on chest X-ray; quantitative PCR using skin biopsy (sensitivity 81%), borreliacidal antibody test (sensitivity 79%, specificity 100%), acute + convalescent phase serology (sensitivity 68%), nested PCR (sensitivity 64%); circulating immune complexes during erythema chronicum migrans; patients with increased IgM and cryoglobulins containing IgM at risk of developing arthritis; cryoglobulins and immune complexes found in synovial fluid, but not serum, during arthritis

Treatment:

Erythema Chronicum Migrans: tetracycline 250 mg orally 6 hourly (child after completion of dentition:

40 mg/kg to 1 g orally daily) for 10-20 d; phenoxymethylpenicillin 500 mg orally 6 hourly (< 12 y: 25-50 mg/kg orally daily in 4 divided doses) for 10-20 d, erythromycin 250 mg orally 6 hourly (younger children: 30 mg/kg to 1 g orally daily in divided doses) for 10-20 d, doxycycline 1-2 mg/kg to 100 mg twice a day, amoxycillin 50 mg/kg/d to 1500 mg/d in 3 divided doses, cefuroxime axetil 10-15 mg/kg to 500 mg twice a day, clarithromycin 500 mg twice a day, azithromycin 500 mg on day1 and then 250 mg 4 times a day

Arthritis: doxycycline 100 mg orally 12 hourly for 3-4 w, amoxycillin 500 mg orally 8 hourly (child: 40 mg/kg orally daily in 3 divided doses) for 4 w, ceftriaxone 2 g (child: 50-80 mg/kg) i.v. daily for 14-21 d, benzylpenicillin 20-24 MU (child: 250,000-400,000 U/kg) i.v. daily in divided doses for 21 d, benzathine penicillin 2.4 MU i.m. weekly for 3 w

Bell's Palsy, Mild Cardiac Disease: doxycycline 100 mg orally 12 hourly for 4 w, amoxycillin 250-500 mg orally 8 hourly (child: 20-40 mg/kg orally daily in 3 divided doses) for 4 w, cefuroxime axetil 10-15 mg/kg to maximum 500 mg twice a day, macrolides

Meningoencephalitis, Heart Block: oral prednisone + ceftriaxone 2 g (child: 50-80 mg/kg) i.v. daily for 14 d or benzylpenicillin 20-24 MU (child: 250,000-400,000 U/kg) i.v. daily in divided doses or oral or i.v. doxycycline

Prophylaxis: vaccine 79-92% efficacy (not cost effective unless prevalence > 2% per season)

REITER SYNDROME (ARTHRITIC SPIROCHAETOSIS, BLENORRHAGIC ARTHRITIS, CONJUNCTIVOURETHRAL-SYNOVIAL SYNDROME, ENTEROARTICULAR SYNDROME, FIESSINGER-LEROY-REITER SYNDROME, INFECTIOUS UROARTHRITIS, NONGONOCOCCAL URETHRITIS WITH CONJUNCTIVITIS AND ARTHRITIS, OCULOURETHROARTICULAR SYNDROME, POSTDYSENTERIC RHEUMATOID, POSTDYSENTERIC SYNDROME, POSTENTERIC RHEUMATOID, REITER DISEASE, REITER TRIAD, REITER RHEUMATISM, SPIROCHAETOSIS ARTHRITICA, URETHRAL ARTHRITIS, URETHRAL RHEUMATISM, URETHROARTHRITIS, URETHROOCULOARTICULAR SYNDROME, URETHROOCULOSYNOVIAL SYNDROME, WAELSCH URETHRITIS)

Agents: unknown; has followed epidemics of diarrhoea due to *Shigella*, *Salmonella, Yersinia* and *Cyclospora*; gonococcal and nongonococcal urethritis (especially that due to *Chlamydia trachomatis*) is also a common antecedent, particularly in young males having HLA B27 histocompatibility antigen

Diagnosis: triad of inflammatory oligoarthritis, ocular inflammation and sterile urethritis; may be fever, ulceration of glans penis (balanitis circinata) and oral mucosa, palmar and plantar lesions (keratodermia blenorrhagica), nausea, anorexia, erythema, myocarditis, pericarditis, neuritis

Treatment: symptomatic

WHIPPLE'S DISEASE: rare (< 1000 cases worldwide reported to date) systemic infectious disease; 97% Caucasian

Agent: *Tropheryma whippelii*

Diagnosis: arthralgia (initial presentation in 67%), epigastric pain (initial presentation in 15%), lethargy, anemia and low grade fever (initial presentation in 14%), neurological symptoms (initial presentation in 4%); later, diarrhoea with fetid, watery, steatorrhoeic stools, malabsorption of fat, protein, carbohydrate, vitamins and minerals, and weight loss in 85%; hyperpigmentation; progresses to cardiac and neurological deficits (headaches, lethargy, visual disturbances, auditory disturbances, gait disturbances, disturbed sleep, impotence, convulsions) and occasionally eye problems (edema in papilla, retinal bleeding, uveitis, corneoretinitis, keratitis); immunohistochemical analysis or PCR of tissue; PCR of CSF, peripheral blood; multiple rounded or sickle-shaped PAS diastase resistant inclusions in lamina propria macrophages in small bowel biopsy

Differential Diagnosis: AIDS, Crohn's disease, disseminated histoplasmosis, immunocomplex disease, immunodeficiency disease, infectious arthritis (shigellosis, salmonellosis, yersinosis, *Campylobacter* infection, amoebiasis), macroglobulinemia Waldenström, *Mycobacterium avium-intracellulare* infection, neoplasia (especially non-Hodgkin's lymphoma), rheumatoid arthritis, *Corynebacterium equi* infection, sarcoidosis, ulcerative colitis, prodromal stage of measles (Warthin-Finkeldey giant cells), malakoplakia (Michaelis-Gutmann bodies staining for calcium and iron in macrophages)

Treatment: parenteral cotrimoxazole or streptomycin 1 g/d + benzylpenicillin 1.2 MU/d for 2 w, then cotrimoxazole 160/800mg for 1-2 y

SARCOIDOSIS (BENIGN LYMPHOGRANULOMATOSIS, BESNIER-BOECK-SCHAUMANN DISEASE, BESNIER-BOECK-SCHAUMANN SYNDROME, BOECK DISEASE, BOECK LUPOID): generalised granulomatous disease; may affect any part of body but, most frequently, lesions are found in lymph nodes, liver, spleen, lungs, skin (Besnier-Boeck disease, Boeck sarcoid, Hutchinson-Boeck disease), eyes, tonsils and bone marrow; causes defects in cell-mediated immunity, with increased susceptibility to *Mycobacterium tuberculosis, Nocardia* and fungi

Agent: ? *Mycobacterium* species

Diagnosis: clinical; histology and immunohistology

Treatment: steroids

CANDIDIASIS (MONILIASIS): ≈ 240 deaths/y in USA; bronchopulmonary, cutaneous, genital, oral, urinary, endocarditis, chronic and sub-acute fever

CHRONIC MUCOCUTANEOUS CANDIDIASIS: T-cell immunodeficiency (fairly specific—*Candida* and some antigenically close fungal genera; thus different from other known immunodeficiencies; since other host defences are normal, systemic candidal infection is not a problem); candidal infection of mucous membranes, skin, hair and nails; endocrinopathy in ≈ 50% (usually several years after candidiasis; most common hypoparathyroidism, Addison's disease; cause autoantibodies); familial in ≈ 20%; other manifestations autoimmunity (eg., pernicious anemia, alopecia, depigmentation, iron-deficiency anemia); early onset chronic mucocutaneous candidiasis most severe form, hypoparathyroidism and Addison's disease very rare; late onset chronic mucocutaneous candidiasis mild, in older individuals, no endocrinopathies; familial chronic mucocutaneous candidiasis autosomal recessive, mild to moderate, endocrinopathies uncommon; juvenile familial endocrinopathy with candidiasis mild to moderate, hypoparthyroidism and/or Addison's disease usually present; other predisposing conditions diabetes mellitus, oral contraceptives, broad spectrum antimicrobials, treatment with immunosuppressive drugs, ? gastrointestinal reservoir

Agent: *Candida*

Diagnosis: micro (wet film, Gram stained film) and culture of appropriate specimen

Treatment: ketoconazole 200-400 mg orally daily, fluconazole 50-100 mg orally daily

SYSTEMIC CANDIDIASIS: associated with antibiotic administration, intravenous or intraarterial catheters or needles, corticosteroid administration (infection in brain and kidneys), use of immunosuppressive agents, neutropenia (disseminated infection), parenteral nutrition (eye may be affected), ambulatory peritoneal dialysis (peritonitis reported), heroin addiction (septicemia followed by folliculitis, bone and joint lesions, ocular abnormalities such as abscess or hypopyon), AIDS

Agent: *Candida*

Diagnosis:

Acute: cutaneous lesions, myositis, myocarditis, acute renal failure, pulmonary infiltration (often multiple), hypotension, fungemia, granulocytopenia, high mortality despite therapy

Chronic: calcified hepatic and splenic abscesses, lesions usually detectable on computerised axial tomography and magnetic resonance imaging during granulocytopenia, elevated level of serum alkaline phosphatase, low mortality urine micro (blastospores and hyphae in ≈ 1/3) and culture (≈ 80% positive), arterial blood culture (biphasic medium), sterile site culture or smear; precipitin test; agglutination titre (commercially available antigen), counterimmunoelectrophoresis (sensitivity 58%, specificity 96%), immunodiffusion (restricted availability; detects antigen and antibody)—all highly controversial tests with many false positive and negative results; antigen in urine or serum experimental; ELISA (antigen, antibody), latex agglutination, radioimmunoassay (sensitivity 71%, specificity 66%), indirect hemagglutination (sensitivity 97%, specificity 60%), indirect immunofluorescence (sensitivity 91%, specificity 50%); increased arabinitol/creatinine ratio experimental

Treatment: ketoconazole 200-400 mg orally (< 20 kg: 50 mg; 20-40 kg: 100 mg) once daily, fluconazole 200-400 mg (child: 1-4 mg/kg) orally daily, amphotericin B under expert supervision ± flucytosine (not *Clavispora lusitaniae*); removal of catheters, needles, prostheses, valves and vegetations

Secondary Prophylaxis and Maintenance: fluconazole 50-200 mg orally daily, ketoconazole 200 mg orally daily

DISSEMINATED *TRICHOSPORON* INFECTION: nonspecific febrile illness or pneumonia in immunosuppressed (especially neutropenic) patients (especially with acute myelogenous leukemia); lungs, liver, spleen, blood, urine, bone marrow, kidney, skin, heart, trachea, esophagus, adrenal; case-fatality rate 74%

Agent: *Trichosporon beigelii, Trichosporon asahii*

Diagnosis: blood cultures, culture and histology of specimens

Treatment: amphotericin B 1-1.5 mg/kg/d + flucytosine 800 mg/d; fluconazole; itraconazole for 20 mo in chronic cases

DISSEMINATED COCCIDIOIDOMYCOSIS: rare (7% of total); more common in infants, elderly, male, Filipino, African-American, native American, Hispanic, Oriental, and patients with impaired immunity (second ½ of pregnancy and postpartum, malignancy, chemotherapy, steroid use, seropositive for *human immunodeficiency virus*); skin (most common), meninges (most serious, 40% case-fatality rate), viscera (liver, spleen, prostate, adrenals), bones and joints, lymph nodes, serous membranes (peritoneum, pericardium)

Agent: *Coccidioides immitis*

Diagnosis: fever in 95%, pulmonary disease in 90%, weight loss in 60%, anemia in 50%, hepatosplenomegaly in 10-20%, meningitis in 10%, skin lesions in 5%; antibody detection often unreliable in immunocompromised host; EIA using a combination of antigens method of choice; latex agglutination (IgM) detects early acute disease, false positive results occur, positive results must be confirmed with immunodiffusion tube precipitin or immunodiffusion complement fixation test; immunodiffusion tube precipitin test (IgM) useful for diagnosis of early acute illness; immunodiffusion complement fixation test (IgG) useful for diagnosis of localised and disseminated disease, qualitative screen, may be quantitative; complement fixation test (IgG) diagnostically and prognostically valuable, titres of 1:8 diagnostic, changes in titres diagnostic, when titres of 1:2-1:8 are revealed confirmation by immunodiffusion complement fixation test necessary; coccidioidin skin test; negative skin test and serum complement fixation test titre > 1:66 indicate large likelihood; micro (30-80 μm round spherules containing 2-5 μm endospores reproducing by fission) and culture of appropriate specimen obtained directly from tissues affected or fluid from these tissues

Treatment:

Meningitis:

Induction:

Severe: i.v. amphotericin B up to 1.5 mg/kg/dose + amphotericin B + hydrocortisone intrathecally

Mild: fluconazole

Maintenance: fluconazole

Skin, Lymph Nodes: amphotericin B 1-1.5 mg/kg/d to total 1.5-2 g i.v. ± local irrigation with 10% solution or local paste and/or excision

Bones, Viscera, Genitourinary Tract, Peritonitis:

Severe or Potentially Severe Disease: amphotericin B (1-1.5 mg/kg (initial up to 50 mg) i.v. to total 1-3 g ± local irrigation and/or surgery

Mild to Moderate Stable Disease: ketoconazole 400 mg orally for 3 mo to several years, fluconazole 400 mg orally initial then 400-800 mg for 3 mo to several years, itraconazole 400 mg orally

Nondisseminated Extracutaneous Disease in Immunocompetent Host: ketoconazole

CRYPTOCOCCOSIS (EUROPEAN BLASTOMYCOSIS, TORULOSIS): sporadic, worldwide; incidence 8/M/y in Australia (from 2/M/y in Tasmania to 44/M/y in Northern Territory); associated with HIV (50%) and other immunodeficiency (21%; Hodgkin's disease, sarcoidosis, collagen disease, carcinoma, treatment with corticosteroids and immunosuppressive agents, adrenal hyperplasia, renal transplantation under treatment with azathioprine and corticosteroids); meningitis, pneumonia, pericarditis, hepatic failure, osteomyelitis, arthritis, subcutaneous and cutaneous lesions, paravertebral abscesses and cord compression, muscle weakness

Agent: 84% *Cryptococcus neoformans* var *neoformans,* 12% *Cryptococcus gattii*, 5% unknown biotype, rarely *Cryptococcus albidus, Cryptococcus laurentii*

Diagnosis: India ink micro preparation (positive in 33-60%), culture (usually growth in 4-7 d, may take 4-6 w or require hypertonic medium) of spinal fluid (46-100% positive), blood (lysis-centrifugation blood culture; 48-89% positive), bronchoalveolar lavage (75-100% positive), pus, sputum (50% positive), pleural fluid (50% positive), urine (17% positive), peritoneal dialysate (100% positive), bone marrow (100% positive); latex slide agglutination test (commercially available) for antigen in CSF, blood, urine (positive in 86-90%; may be positive when India ink test is negative; highly sensitive and specific for diagnosis of meningeal and disseminated forms; prozone-like effect controlled by dilution of specimen or treatment with pronase; rare false negatives with capsule-deficient *Cryptococcus neoformans* in patients with AIDS; rare false positives with *Capnocytophaga canimorsus* septicemia, patients with malignancy, *Trichosporon beigelii* disseminated infection); tube agglutination, charcoal particle agglutination, indirect fluorescent tests for antibody in serum (positive in 28%); complement fixation test; meningitis: CSF cells usually < 800/μL, either neutrophils or lymphocytes predominating, protein increased (rarely > 800 mg/dL), glucose decreased, chloride < 105 mEq/L

Treatment:

Mild: fluconazole 800 mg orally or i.v. initially, then 400 mg daily for 10 w

More Severe: amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 2-4 w ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 2-4 w; if clinical improvement after 2 w, change to fluconazole 800 mg orally initially then 400 mg daily for 8 w

Secondary Prophylaxis in HIV Infection: fluconazole 200 mg orally daily or itraconazole 200 mg orally daily

TORULOPSOSIS: superinfection during treatment with cytotoxic and/or immunosuppressive drugs + corticosteroids (similar to systemic candidiasis) and in diabetes mellitus, particularly with acidosis (pyelonephritis; occasionally pneumonia and/or empyema)

Agent: *Candida glabrata*

Diagnosis: direct mount and culture of urine, sputum

Treatment: amphotericin B ± flucytosine

GEOTRICHOSIS: neutropenic leukemics; blood, urine, skin, lungs, heart, liver, spleen, lymph nodes, bone marrow, kidney

Agent: *Geotrichum candidum*

Diagnosis: micro and culture of sputum, pus from oral lesions, feces

Treatment: amphotericin B

BLASTOMYCOSIS (GILCHRIST'S DISEASE, NORTH AMERICAN BLASTOMYCOSIS): uncommon, sporadic in N and Central America, recently recorded in Spain; transmission by inhalation; 75% of patients not immunocompromised

Agent: *Ajellomyces dermatitidis*

Diagnosis: microscopy (visualisation of buds in wet preparation) and culture of scrapings from cutaneous lesions and pus from abscesses on periphery of lesion, sputum, urine, CSF; complement fixation test (usually positive only in systemic disease; sensitivity 40%, specificity 100%; predictive value positive 100%, predictive value negative 81%), immunodiffusion

(sensitivity 66%, specificity 100%, predictive value positive 100%, predictive value negative 88%) and skin tests (frequently unhelpful), ELISA using purified antigen A (sandwich sensitivity 88%, specificity 100%, predictive value positive 100%, predictive value negative 98%; indirect sensitivity 80%, specificity 94%, predictive value positive 94%, predictive value negative 93%; false positives in some cases of histoplasmosis and sporotrichosis), radioimmunoassay (sensitivity 85%, specificity 100%, predictive value positive 100%, predictive value negative 92%); hypochromic anemia with neutrophilia, raised erythrocyte sedimentation rate

Treatment:

Mild Cases: itraconazole, ketoconazole 200-800 mg orally daily for up to 1 y, amphotericin B to total dose of 2 g

Severe Cases: amphotericin B under expert guidance, hydroxystilbamidine if amphotericin B fails

HISTOPLASMOSIS: reported from 130 widely scattered countries; endemic in Ohio Valley, Mississippi Valley and Appalachian Mountains; in Australia, patients infected from a chicken coop and associated with a cave in NSW; 'cave disease' contracted by visitors to caves inhabited by bats; African form in endemic belt through central Africa; ≈ 300 cases (≈ 60 deaths)/y in USA; 50-99% asymptomatic, 1-50% self-limited; pulmonary infections (tuberculosis-like disease of lungs; acute 60% of symptomatic, chronic 10%), pericarditis (10% of symptomatic), disseminated (immune defect, leukemia, Hodgkin's disease; in 75% of symptomatic patients on immunosuppression (especially steroids); < 0.5% of AIDS patients; 10% of symptomatic patients overall), arthritis and erythema nodosum (5% of symptomatic), bone marrow infections, endocarditis, oronasopharyngeal lesions, lymph gland infections, mediastinal granulomas, meningitis (8% of cases in AIDS and ¼ of those with disseminated disease)

Agent: *Histoplasma capsulatum var capsulatum*, *Histoplasma capsulatum var duboisi* (tropical Africa; predilection for visceral involvement, higher case-fatality rate)

Diagnosis: incubation period > 21 d; fever in 95%, weight loss in 90%, anemia in 70%, pulmonary disease in 50%, hepatosplenomegaly in 25%, lymphadenopathy in 20%, skin lesions in 5-10%, meningitis in < 1%; microscopy (1-5 μm round to oval budding cells; rapid but low sensitivity and identification errors) and culture (insensitive in cases of self-limited disease, may require 2-4 w of incubation to produce growth, may require invasive procedure for obtaining specimen) of material from cutaneous and mucosal lesions, sputum, gastric washings, biopsy of oronasopharyngeal lesions, lymph glands, bone marrow; serological tests for antibody sensitive in chronic and self-limited disease, falsely negative early in infection, falsely positive in cases of other fungal disease, may remain positive for years; HP antigen detection sensitive (80-92%) in cases of disseminated disease but poor sensitivity in chronic and self-limited disease, rapid turnaround time, level of HP antigen decreases after treatment, increases with relapse); immunodiffusion (active cases 2% H positive, 10% H and M positive; 70% of all cases M positive; detection of M precipitin may be influenced by skin test), complement fixation test (commercially available; yeast antibody 90% sensitivity, nonspecific at low titres; histoplasmin antibody 80% sensitivity, more specific; skin test may interfere), latex agglutination (detects early acute disease, most chronic cases negative), radioimmunoassay detection of antigen in serum and in urine (disseminated cases 90% urine and 50% serum positive, valuable for immunodeficient patients; nondisseminated cases urine 50-75% negative, some cross-reactivity); skin test not useful diagnostically, useful epidemiologically, may confuse interpretation of serological tests by presence of booster effect; hypochromic anemia with leucopenia; in children, lymphocytosis with atypical mononuclears

Disseminated: fever in 70% of cases, weight loss in 66%, pulmonary symptoms in 50%, thrombocytopenia in 50%, anemia in 45%, splenomegaly in 40%, oral lesions in 25%, leucopenia in 25%, neurologic symptoms in 20%, leucocytosis in 10%; positive cultures from 90% of oral lesions, 70% of lymph nodes, 70% of bone marrows, 60% of sputum specimens, 55% of liver biopsies (granulomas in 70%, organism seen microscopically in 40%), 55% of blood cultures, 45% of CSF specimens and 45% of urine specimens; 1/3 of patients with negative blood cultures have positive bone marrow; none with negative bone marrow have positive blood culture; 40% of patients with positive urine culture have normal renal function

Treatment: not indicated in acute pulmonary, pericardial, rheumatologic, coin lesions, fibrous mediastinitis; indicated in disseminated, chronic pulmonary, acute respiratory distress syndrome, symptomatic mediastinal granuloma, persistent (> 1 mo) acute pulmonary

Induction:

Mild: itraconazole 400 mg/d for 3 mo, fluconazole 800 mg/d for 3 mo

Severe: amphotericin B 0.7 mg/kg/d to 50 mg/d + prednisone 60 mg daily for 2 w

Maintenance: itraconazole 200-400 mg/d for 12 w (acute pulmonary), 12-24 mo (chronic pulmonary), 6-18 mo (disseminated in non-AIDS), life (disseminated in AIDS), 6-12 mo (granulomatous mediastinitis); fluconazole 400 mg/d for life

Nondisseminated Extracutaneous Disease in Immuncompetent Host: ketoconazole 400 mg orally (child < 20 kg: 50 mg; 20-40 kg: 100 mg, > 40 kg: 200 mg) daily for 6-12 mo, cotrimoxazole 160/800 mg orally 12 hourly for 4-5 w

PARACOCCIDIOIDOMYCOSIS (KUTZ-SPLENDORE-DE ALMEIDA'S DISEASE, SOUTH AMERICAN BLASTOMYCOSIS): restricted to S America and Central America, including Mexico; may not appear till long after acquisition; mucous membrane of mouth most frequently affected area; lymph nodes affected in almost all cases; lungs affected in high proportion of cases

Agent: *Paracoccidioides brasiliensis*

Diagnosis: microscopy and culture of scrapings from affected skin (paracoccidioidal granuloma) and mucous membranes, pus from fluctuant nodules, sputum; complement fixation test (usually positive only in systemic cases); iron deficiency anemia with neutrophila and raised erythrocyte sedimentation rate; eosinophlia sometimes

Treatment: ketoconazole 400 mg (child < 20 kg: 50 mg; 20-40 kg: 100 mg; > 40 kg: 200 mg) orally daily for 3 mo then 200 mg daily for 9-12 mo, sulphonamides, amphotericin B under expert supervision then maintenance ketoconazole as above, miconazole

SPOROTRICHOSIS: worldwide; up to 1/1000 in rural areas of Central and S America; cutaneous lymphatic (most common form; firm subcutaneous nodules), fixed cutaneous (no lymphatic involvement), localised extracutaneous (skeletal most common; pulmonary can mimic tuberculosis), disseminated (rare; immunosuppressed patients)

Agent: *Sporothrix schenckii*

Diagnosis: wet preparation micro, Gram stain (note that cigar-shaped yeast phase cells may resemble diphtheroids), methenamine silver stain, fungal culture of aspirate or purulent exudate or biopsy of cutaneous or mucosal lesion, sputum, bronchial aspirate, lung biopsy, synovium, synovial fluid; blood cultures; serology (latex agglutination, tube agglutination)

Treatment:

Cutaneous-lymphatic Form: surgery; potassium iodide up to 3-4 g 8 hourly as a saturated (1 g/mL) solution continuing for 1 mo after clinical cure, ketoconazole 200-400 mg orally (< 20 kg: 50 mg; 20-40 kg: 100 mg) daily for 3-6 months, itraconazole 100 mg orally daily with meals for 120 d (not in pregnancy)

Pulmonary and Disseminated Forms: amphotericin B to total dose 2-3 g, ketoconazole 400-500 mg daily

Maintenance: itraconazole

ASPERGILLOSIS: in farmers, poultry workers and immunocompromised; 151% increase in annual incidence (1.91 to 4.8/M) between 1970 and 1976 in USA; associated with use of corticosteroids and/or antimicrobials, immunosuppressive agents, leucopoenia; acute lymphocytic leukemia in 40% of patients, acute myelogenous leukemia in 20%, chronic myelogenous leukemia in 10%, Hodgkin's disease in 5%, lymphoma in 5%, other diseases of lymphoreticular system (aplastic anemia, chronic lymphocytic leukemia, mycoides fungoides, multiple myeloma) in 10%, 'autoimmune' disease (systemic lupus erythematosus, polyarteritis nodosa) in 5%; 95% lung, 20-70% gastrointestinal tract, 15-50% brain, 10-40% liver, 10-40% kidney, 10-30% thyroid; also heart, sinus, eye, spleen, diaphragm, tongue, testis, rare meningitis in AIDS

Agents: *Aspergillus fumigatus* (75%), *Aspergillus flavus*, *Aspergillus glaucus, Aspergillus terreus, Aspergillus ustus*

Diagnosis: visualisation of hyphae; confirmed by culture

Aspergilloma: hyphae in mass in bloody sputum from lung; sputum and biopsy culture

Invasive Aspergillosis: 60% of isolates in allogeneic bone marrow transplant recipient, 60% in neutropenics, 50% in persons with hematological cancer, 30% in malnutrition, 20% in HIV infection, 20% in solid organ transplantation, 20% in corticosteroid users, 10% in those with underlying pulmonary disease; only 38% alive 3 mo after diagnosis; sputum culture in neutropenic patient; KOH preparation and culture of biopsy of sterile site; sandwich ELISA for galactomannan on serum (sensitivity 94%, specificity 85%), counterimmunoelectrophoresis (precipitating antibodies), radioimmunoassay (usually positive), immunodiffusion (restricted availability; positive result suggests diagnosis if serial specimens are obtained), complement fixation test, precipitins; serial quantitative assay for antibodies may be better than culture (recovered from blood in < 5%, cutaneous lesions in < 10%), or attempts to detect antigen in immunocompromised patients; halo sign on CT inidcative of invasive pulmonary aspergillosis

Treatment:

Severe: amphotericin B under expert supervision (rate of response 55%) ± flucytosine or rifampicin; reduce immune suppression

Mild or Moderate: itraconazole

***NEOSARTORYA* INFECTIONS:** occasional opportunistic infections

Agents: *Neosartorya fischeri* systemic infection in transplant recipients, mixed pulmonary infection in patient with multiple myeloma; *Neosartorya pseudofischeri* localised and invasive infections; *Neosartorya hiratsukae* cerebral infection

Diagnosis: visualisation of hyphae; confirmed by culture

Treatment: itraconazole 400 mg daily

ZYGOMYCOSIS: lung, spleen, kidney, CNS, gastrointestinal tract, heart, sinus, eye, liver, pancreas; rhinocerebral associated with diabetes mellitus (with or without associated acidosis or hyperglycemia; 75% of cases), hematological neoplasia, malnutrition, severe (third degree) burns, immunosuppression, following homotransplantation, uremia; cerebral associated with pulmonary or disseminated fungal infection, hematolgic malignancy; pulmonary associated with leukemia, lymphoma and leucopenia (75% of cases), diabetes mellitus (with or without associated acidosis or hyperglycemia), renal failure, third degree burns, corticosteroid therapy, cytotoxic therapy; gastrointestinal rare, associated with protein-calorie malnutrition (especially children in tropical and subtropical countries with kwashiorkor), diabetes mellitus, hematological malignancy, uremia, acidosis due to diarrhoea, amoebic colitis, therapy with corticosteroids, ulcerative colitis, abdominal surgery; disseminated associated with leukemia, lymphomas, anmias, multiple myeloma, solid tumours, agranulocytosis, uremia, third

degree burns, intravenous narcotic abuse, hemodialysis and deferroxamine, organ transplantation, wounds, neonatal state, lung disease; cutaneous associated with diabetes mellitus, burns, under Elastoplast dressings, AIDS; localised following surgery rare—brain abscess following neurosurgery, prosthetic valve, vascular graft; renal associated with chronic or acute renal failure

Agents: *Rhizopus*, *Absidia*, *Mucor*, rarely *Cunninghamella elegans, Cunninghamella bertholetiae, Basidiobolus haptosporus*

Diagnosis: temperature > 38.3°C in 61% of cases; histology and culture of infected tissue (necrotic lesion or sterile site)

Treatment: aggressive surgical debridement; amphotericin B 1 mg/kg/d i.v. for 2-3 mo; control of underlying predisposing conditions (diabetes, immunosuppression, immunodeficiency); hyperbaric oxygen

PENICILLIOSIS: in acute lymphoblastic leukemia; focal infections and fatal, progressive disseminated infection (lungs, heart, blood, mediastinum, superior vena cava)

Agent: *Penicillium*, including *Penicillium marneffei* in AIDS (geographic distribution limited to SE Asia)

Diagnosis: fever in 99%, weight loss in 75%, anemia in 75%, skin lesions in 70%, pulmonary disease in 50%, hepatosplenomegaly in 50%, lymphadenopathy in 40-50%, meningitis very rare; Grocott methenamine silver, periodic acid Schiff and Wright's staining (1-8 μm pleomorphic elongated cells reproducing by fission) and culture at 25°C and 37°C of biopsies, bone marrow aspirate, touch smears of skin specimens

***Penicillium marneffei*:** fever, marked weight loss, anemia, generalised papular skin lesions, lymphadenopathy, hepatomegaly

Treatment:

Severe: amphotericin B

Mild: itraconazole; flucytosine 150 mg/kg/d + ketoconazole 400 mg/d for 90 d

Maintenance: itraconazole

FUSARIOSIS: in immunocompromised, especially acute leukemia; skin, lung, blood, kidney, sinus, eye, gastrointestinal tract, heart, spleen, CNS, liver, pancreas, urine, i.v. line tip, bone marrow, testis; death rate approaching 100%

Agents: *Fusarium solani, Fusarium oxysporum, Fusarium chlamydosporum, Gibberella fujikuroi, Fusarium anthophilum, Gibberella intermedia*

Diagnosis: persistent fever, skin lesions (ecthyma-like lesions, target lesions, multiple subcutaneous nodules; 60% of patients), orbofacial involvement, fungemia, myalgias; blood cultures positive in 60%; histology and culture of skin biopsies

Treatment: control of underlying disease and recovery from neutropenia (granulocyte infusions + GM-CSF); surgical resection; voriconazole; amphotericin B 1.0-1.5 mg/kg daily, liposomal amphotericin B 5-15 mg/kg daily

TRICHOTHECENE MYCOTOXINS: used as biowarfare agents

Agent: *Fusarium*

Diagnosis: cutaneous exposure causes rapid erythema, blistering and necrosis of skin; eye exposure causes tearing, conjunctivitis and blurred vision; respiratory exposure causes nasal burning and epistaxis, sore throat, cough, dyspnoea and chest pain; high doses cause nausea, burning skin, lethargy and incoordination within minutes, bleeding, cough, dyspnoea, chest and abdominal pain, diarrhoea and blistering of skin within hours; severe poisoning causes extensive mucosal bleeding, hypothermia and shock; gas chromatography, mass spectrometry, ELISA or radioimmunoassay on urine

Treatment: none proven; gastric infusion of activated charcoal and high doses of corticosteroids beneficial in mice

Prevention: protective clothing and face masks

SYSTEMIC *HANSENULA* INFECTIONS: immunosuppression, use of intravenous device, previous treatment with antibacterial drugs; 59% from blood, 18% from CSF, 6% from mediastinal lymph nodes, 6% from endocardium, 6% from kidney, 6% from spleen

Agents: 92% *Hansenula anomala*, 8% *Pichia angusta*

Diagnosis: blood cultures, histology and culture of biopsy specimens

Treatment: amphotericin B

SYSTEMIC *BIPOLARIS* INFECTIONS: in multiple myeloma; sinus, lungs

Agent: *Bipolaris*

Diagnosis: histology and culture of biopsy specimens

Treatment: amphotericin B (usually not successful), itraconazole

SYSTEMIC *PSEUDALLESCHERIA BOYDII* INFECTIONS: cancer patients on steroids, chronic pulmonary disease, hematological malignancy during therapy, neutrophil dysfunction, near-drowning; heart, blood, brain, lungs, kidney

Agent: *Pseudallescheria boydii*

Diagnosis: culture of blood, sputum and urine

Treatment: ketoconazole, fluconazole, flucytosine

***SACCHAROMYCES CEREVISIAE* INVASIVE INFECTIONS:** severe immunosuppression, prolonged hospitalisation, prior antibacterial therapy, prosthetic cardiac valves; pneumonia, liver abscess, sepsis, disseminated infection with cardiac tamponade

Agent: *Saccharomyces cerevisiae*

Diagnosis: smear and culture of biopsy

Treatment: amphotericin B to total dose 300-1400 mg

SYSTEMIC *DIPODASCUS CAPITATUS* INFECTIONS: leukemia; pneumonia, focal infection of liver, spleen, kidney, brain, skin, oesophagus, stomach, bacteremia, myocarditis, endocarditis

Agent: *Dipodascus capitatus*

Diagnosis: blood cultures; smear and culture of sputum, sinus, biopsy

Treatment: prolonged amphotericin B + flucytosine

SYSTEMIC *EXOPHIALA DERMATATIDIS* INFECTION: pneumonia, brain abscess; chronic granulomatous disease

Agent: *Exophiala dermatitidis*

Diagnosis: micro and culture of biopsy

Treatment: surgical resection of pulmonary lesion; amphotericin B, flucytosine, ketoconazole + transfused white cells, followed by prolonged course of fluconazole

SCEDOSPORIOSIS: posttraumatic cellulitis, septic arthritis and osteomyelitis, oncychomycosis, otomycosis, fungal balls in paranasal sinuses, lungs and bronchi in immunocompetent; endophthalmitis in i.v. drug use; systemic infection (endophthalmitis, endocarditis, metastatic abscesses) in immunocompromised

Agents: *Scedosporium apiospermum, Scedosporium prolificans*

Diagnosis: micro and culture of appropriate specimen

Treatment: surgery; itraconazole; amphotericin B in lipid 5-15 mg/kg/d

SYSTEMIC PROTOTHECOSIS: gallbladder, liver, duodenum

Agents: *Prototheca wickerhamii, Prototheca zopfii*

Diagnosis: elevated IgG, elevated erythrocyte sedimentation rate, eosinophilia, raised liver enzymes; microscopy and culture of biopsy, stool

Treatment: short course of amphotericin B followed by oral ketoconazole for 3 mo

DISSEMINATED *PNEUMOCYSTIS JIROVECI* INFECTION: AIDS, hematolgic malignancy, lymphoreticular malignancy, immunosuppressive therapy; 46% lymph nodes, 36% bone marrow, 36% spleen, 32% liver, 18% gastrointestinal tract, 18% retina, 16% adrenal, 16% thyroid, 14% kidneys, 12% vessels, 10% heart, 8% pancreas, 6% external auditory canal, 4% brain, 4% thymus, 4% pleura, 2% middle ear/mastoid, 2% hard palate, 2% ureters, 2% Virchow-Robin spaces, 2% diaphragm, 2% pericardium, 2% retroperitoneal tissue

Agent: *Pneumocystis jiroveci*

Diagnosis: Wright-Giemsa, Papanicolau, Gomori methenamine silver stain, direct immunofluorescence of appropriate specimen

Treatment: cotrimoxazole 5/25 mg/kg oral or i.v. 6-8 hourly for 3 w then 80/400-160/800 mg orally daily or 160/800 mg orally 3 or 4 d/w or 12 hourly 2 d/w; pentamidine isethionate 4 mg/kg to 300 mg i.v. daily for 3 w then 300 mg i.v. or aerosolised every 2-4 w

Maintenance Therapy in HIV/AIDS: cotrimoxazole 80/400-160/800 mg orally daily or 160/800 mg orally 3 times weekly, dapsone 100 mg orally 3 times weekly, pentamidine 300 mg i.v. or aerosolised every 2-4 w

Prophylaxis (CD4 Cell Count < 200/μL): cotrimoxazole 80/400-160/800 mg orally daily or 160/800 mg orally 3-4 times a week or 12 hourly twice a week, pentamidine 300 mg i.v. or aerosolised every 2-4 w, dapsone 100 mg orally 3 times a week

VISCERAL LEISHMANIASIS (ASSAM FEVER, BUNDWAN FEVER, CACHECTIC FEVER, CACHEXIAL FEVER, DEATH FEVER, DUM-DUM FEVER, INFANTILE LEISHMANIASIS, KALA-AZAR, NONMALARIA REMITTENT FEVER, PONOS, SAHIB DISEASE): endemic in 62 countries including India, Mediterranean, East Africa, Middle East, S Africa, China, Latin America; 500,000 new cases/y worldwide, with 41, 000 recorded deaths; human (only reservoir for *Lesihmania donovani donovani*), dog, fox, rodent, jackal reservoirs; transmission by sandfly (*Phlebotomus* and *Lutzomyia*) bite; incubation period weeks to months; untreated cases usually fatal

Agents: *Leishmania donovani* (India and East Africa), *Leishmania chagasi* (New World), *Leishmania nfantum* (Mediterranean); rarely, *Leishmania tropica*

Diagnosis: incubation period > 21 d; prolonged or intermittent fever, marked splenomegaly, hepatomegaly, intermittent cough, diarrhoea, malaise, poor weight gain, wasting; if cell-mediated immunity isufficient, disease may be mild or asymptomatic, with limited pathology; geographic history; history of sandfly bites; fever, splenomegaly; anti-K39 IgG strip test on fingerstick blood (sensitivity 100%, specificity 98%), ELISA (sensitivity 98%, specificity 100%), PCR, examination of splenic pulp smears (positive in 98%), bone marrow smears (positive in 90%), liver biopsy (positive in 70%), thin smears of buffy coat of blood (positive in 60%), lymph node aspirate or biopsy; histological appearances of chronic infection of reticuloendothelial system with presence of parasites in bone marrow, liver, lymph nodes and spleen; culture of tissue or blood; indirect hemagglutination titre, direct agglutination titre, complement fixation test, latex agglutination, Montenegro skin test; progressive anemia with leucopenia and thrombocytopenia, falling serum albumin, greatly increased γ-globulin, raised erythrocyte sedimentation rate and serum viscosity and, later, serum bilirubin

Treatment: meglumine antimonate 20 mg antimony/kg/d for 20-40 d, amphotericin B 7-20 mg/kg total dose i.v. for up to 20 d, liposomal amphotericin B 10-20 mg/kg total dose i.v. in 5-10 doses over 10 d, amphotericin B colloidal suspension 10-15 mg/kg total dose over 5 d, pentamidine 15-30 doses over 3-4 w, miltefosine, metronidazole 25 mg/kg daily i.v. for 5 d, followed by 40 mg/kg orally daily in divided doses for 7 d, sodium stibogluconate 10 mg/kg i.m. or i.v. 8 hourly for 10 d, paromomycin 11 mg/kg i.m. daily for 21 d

VISCERAL LARVA MIGRANS (LARVA MIGRANS VISCERALIS, PARASITIC LARVAL GRANULOMATA, VLM SYNDROME)

Agents: *Toxocara* (toxocariasis, *Toxocara* infection*, Toxocara* infestation*;* principally *Toxocara canis*, less frequently *Toxocara cati*), occasionally *Ascaris lumbricoides, Baylisascaris procyonis* (from raccoons), *Capillaria hepatica, Dirofilaria, Gnathostoma, Toxascaris leonina*

Diagnosis: symptoms depend on number of larvae and on tissues invaded; may be no localised reaction or may be hepatomegaly or hepatosplenomegaly, pneumonitis (tropical eosinophilic pneumonia) or pulmonary infiltrates, allergic phenomena and neural and ocular lesions of varying severity; granulomatous lesions characteristic; fever, rigours, pruritic rash, abnormal behaviour

Toxocara: ELISA, bentonite flocculation (needs evaluation; 1:5 titre may be diagnostic if indirect hemagglutination also positive), indirect hemagglutination (generally reliable although status of disease activity may be uncertain; diagnostic titre 1:400)

Visceral Form: usually benign, but rare deaths due to severe neurologic or myocardial involvement; exposure to dogs and cats or eating raw chicken; 1-5 y old with history of pica; malaise, weight loss, wheezing, cough; surgical liver biopsy; marked eosinophilia (usually > 30%), anemia, neutrophilia in children, increased serum γ-globulin (including increased IgE), raised isohemagglutinin titres

Ocular Form: 5-20 y old; history of pain unusual; failing vision, strabismus, whitish retinal granuloma, endophthalmitis, uveitis; hematological tests usually normal; unnecessary enucleation because of misdiagnosis of retinoblastoma

***Ascaris*:** acute localised manifestations (hepatic, pancreatic, bile duct, intestinal obstruction, peritonitis, appendicitis) and allergic reactions (bronchospasm, pulmonary infiltration, urticaria)

Treatment: corticosteroids in severe cases; thiabendazole 25 mg/kg 12 hourly orally daily for 5 d, diethylcarbamazine 2 mg/kg 8 hourly orally for 7-10 d

VISCERAL GNATHOSTOMIASIS: SE Asia and S America; large range of freshwater fish, amphibians, reptiles, crustaceans, birds and mammals act as second intermediate hosts; pulmonary, gastrointestinal, genitourinary, opthamologic, ear, nose, throat

Agent: *Gnathostoma spinigerum*

Diagnosis: isolation of parasites when possible; eosinophilia; history of travel to SE Asia or S America and ingestion of raw or undercooked fish, poultry or pork

Treatment: removal of worm where appropriate

TRYPANOSOMIASIS

Agents: *Tyrpanosoma brucei gambiense* (Gambian fever, Gambian sleeping sickness, Gambian trypanosomiasis, Mid-African sleeping sickness, West African trypanosomiasis), *Trypanosoma brucei rhodesiense* (East African trypanosomiasis, Rhodesian sleeping sickness, Rhodesian trypanosmiasis; prevalence 12 M), *Trypanosoma cruzi* (American trypanosomiasis, barbeiro fever, Brazilian trypanosomiasis, careotrypanosis, Chagas-Cruz disease, Chagas disease, Chagas-Mazza disease, Cruz trypanosomiasis, South American trypanosomiasis; Central and S America; transmission mostly indoors)

Diagnosis: skin nodule, fever, lymphadenopathy, circinate rash, mental changes; geographic history; insect vector bite (*Glossina* in African trypanosmiasis, reduviid bugs (triatomine (cone nose) bugs of genera *Triatoma, Rhodnius* and *Panstrongylus*) in trypanosomiasis due to *Trypanosoma cruzi*); electrocardiogram (myocarditis); thick and thin blood films and buffy coat examination (febrile stage)

American Trypanosomiasis: incubation period 1-3 w; children 1-5 y old; chagoma (erythematous, warm mass at site of and within few h of bite) persists for 2-3 mo, becomes fibrotic and encapsulated, most commonly on cheek or around eye

Acute: fever, toxic anemia, rash, edema of eyelids with unilateral conjunctivitis, regional adenitis, moderate hepatomegaly or splenomegaly, epistaxis, convulsions, acute myocarditis, cardiac arrhythmias and congestive heart failure, meningoencephalitis

Chronic: fever, adenitis, anemia, monocytosis, weight loss, autonomic neuropathy causing gastrointestinal lesions (megaesophagus, megacolon), myocardial degeneration, biventricular cardiac failure (greater on right than left), meningoencephalitis, pulmonary or systemic embolism

serology (Machado-Geurrein test, indirect fluorescent antibody titre, hemagglutination inhibition test); culture of blood and bone marrow aspirate on biphasic blood agar (NNN) medium; xenodiagnosis (6 clean, uninfected, laboratory-bred reduvid bugs allowed to feed on patient and hindgut examined for epimastigotes after 2 w)

African Trypanosomiasis: incubation period < 21 d; skin nodule (trypanosomal chancre) at site of bite firm, tender, indurated, inflamed, may ulcerate, persists 2-3 w, precedes other manifestations of illness by weeks to years; chills, intermittent fever 2-3 w duration, accompanied by erythematous skin eruption; debilitation, anemia, dyspnoea, edema, headache weeks to months; lymphadenopathy symmetric, predominantly cervical, persists for several months; CNS involvement, muscular pain and spasms, emaciation; hepatosplenomegaly; parasitemia frequently visible on blood smear; early sleeping stage lassitude, apathy, fatigue, later asleep most of time, terminal coma; Kerandel's sign (severe pain over area of nerve distribution following light tap on nerve); Giemsa stained smears of fluid aspirated from an enlarged lymph gland, bone marrow aspirate, CSF; serology (ELISA most sensitive, may give false positives if CSF used; IgM increase in blood and in CSF when nervous system involvement

***Tyrpanosoma brucei gambiense*:** subacute or chronic with mild onset; more severe encephalitis; less visceral involvement; more lymphadenopathy; death in untreated cases usually after several years as result of severe malnutrition and/or intercurrent infections

***Trypanosoma brucei rhodesiense*:** acute with sudden onset and much more acute rapid course; less severe encephalitis; more visceral involvement, including heart; less lymphadenopathy; death in untreated cases usually within weeks or months

Treatment:

Trypanosoma brucei:

Hemolymphatic Stage: suramin 100-200 mg test dose then 1 g (child: 20 mg/kg) i.v. on days 1, 3, 7, 14, 21; *Tyrpanosoma brucei gambiense* only: pentamidine isethionate 4 mg/kg i.m. daily for 10 d

Organisms in CSF: suramin 200 mg test dose i.v. followed by 20 mg/kg to 1 g on days 1, 3 and 8, followed by melarsopol (commencing on day 12) 2-3.6 mg/kg daily for 3 d, course repeated after 1 w at 3.6 mg/kg daily at intervals of 1-5 d for total of 10 doses and 25 mg/kg over 1 mo; nitrofurazone 1-2 g daily in 3 or 4 divided doses for 5-7 days; difluoromethylornithine hydrochloride monohydrate 100 mg/kg 6 hourly infused over 1 h for up to 14 d, followed by 75 mg/kg orally 6 hourly for 30 d

Trypanosoma cruzi: nifurtimox 8-10 mg/kg orally daily in 4 divided doses for 120 d (1-10 y: 15-20 mg/kg daily for 90 d; 10-16 y: 12.5-25 mg/kg daily for 90 d; 50% cure rate), lampit, benzimidazole

Prophylaxis (*Tyrpanosoma brucei gambiense*): pentamidine isethionate 250 mg i.m. given as a single dose

FILARIASIS: 120 M infected worldwide; no deaths reported; Africa, Eastern Mediterranean, Asia, South America; transmission by mosquitoes, infected arthropods; incubation period weeks to years

Agents: *Wuchereria bancrofti, Brugia malayi, Brugia timori, Loa loa, Onchocerca volvulus, Mansonella ozzardi, Mansonella perstans, 'Mansonella streptocerca', 'Meningonema peruzzii', Dirofilaria*

Diagnosis: clinical; bentonite flocculation test (1:5 titre diagnostic if indirect hemagglutination assay also positive), indirect haemagglutination assay (1:400 titre diagnostic if bentonite flocculation test also positive), ELISA (sensitive but non-specific), indirect immunofluorescence; eosinophilia sometimes

***Wuchereria bancrofti*, *Brugia malayi*, *Brugia timori*:** demonstration of microfilariae in peripheral thick blood films taken at night and by histological examination of biopsy material

Acute: recurrent lymphangitis (with *Brugia,* not severe and usually affecting lower limbs with enlargement of femoral and popliteal lymph nodes); may be fever, headache and urticarial rash ('filarial fever')

Chronic: fibrosis and lymphatic obstruction, leading to hydrocele and/or elephantiasis (enlargement of legs, arms, breast and genitals)

Loa loa: adult worms migrate through subcutaneous tissues producing painful transient erythematous inflammation ('fugitive swelling', 'Calabar swelling'), migratory angiedema, urticarial vasculitis, and occasionally across eye beneath conjunctiva; microfilariae in films of peripheral blood collected repeatedly at midday and midnight and concentrated by Knott's technique; occasionally, adult filariae under conjunctiva or in biopsy material of swelling; white cell count 9900/μL, 31% eosinophils

***Onchocerca volvulus*:** chronic; dermatitis (irritating pruritic rash) and sometimes hyperkeratosis, depigmentation; subcutaneous encapsulated tumours (onchocercomata containing adult worm) with muscular pain, sclerosing lymphadenitis, eye disease (conjunctival hyperemia, iritis, corneal opacities, chorioretinitis, optic nerve disease leading to blindness (river blindness)); in Africa, loss of skin elasticity causing hanging groin syndrome; in S America, pouches under eyes causing 'leonine facies'; adult filaria in excised nodules, microfilaria in shavings of skin; histology of lymph nodes; radioimmunoassay; Mazzotti test; patch test

Mansonella: eosinophilia; recovery of microfilariae from blood by Knott's concentration

***Mansonella ozzardi*:** asymptomatic or urticaria, lymphadenopathy, articular pains, pruritic skin eruptions, headaches, hydrocele

***Mansonella perstans*:** usually mild or asymptomatic but can cause arthropathy, Calabar swellings and pyrexia

Mansonella streptocerca: rare; cutaneous edema, rash, red macules

***Meningonema peruzzii*:** acute encephalomyelitis or mild illness with headache, fatigue and drowsiness

***Dirofilaria*:** often asymptomatic; abscesses or nodules ('coin lesions') in heart, lungs, subcutaneous tissue, eye

Treatment: ivermectin 200 μg/kg single oral dose, flubendazole 750 mg i.m. weekly for 5 w, albendazole, diethylcarbamazine

PREVENTION AND CONTROL: control of vectors, treatment of cases

SCHISTOSOMIASIS (BILHARZIASIS, HAEMIC DISTOMIASIS, SNAIL FEVER): worldwide incidence 200 M/y (Africa, Near East, rain forest belt in Central Africa, Western Pacific, Kampuchea, Laos; absent from Australia and Papua New Guinea); dermatitis (within 1-2 d of cercarial penetration), enteritis (*Schistosoma mansoni, Schistosoma japonicum, Schistosoma mekongi, Schistosoma intercalatum, Schistosoma mattheei*), Katayama syndrome (4-8 w after primary infection), urinary infection (chronic *Schistosoma haematobium* infection), intestinal polyps, hepatosplenic schistosomiasis (hepatosplenic bilharziasis; caused by tissue reaction to trapped eggs; varies from formation of a few hepatic granulomas to occurrence of severe hepatosplenic fibrosis, hepatosplenomegaly and portal hypertension), pulmonary schistosomiasis (lung schistosomiasis, pulmonary bilharziasis; caused by a reaction of lung tissues to eggs of *Schistosoma mansoni* and, very rarely, *Schistosoma haematobium* and *Schistosoma japonicum*), CNS schistosomiasis (*Schistosoma mansoni*, *Schistosoma haematobium*, *Schistosoma japonicum*; localisation of granulomata leading to paresis of different types; reported in both acute and chronic stages)

Agents: *Schistosoma mansoni* (Africa, Middle East, S America, Caribbean; mature adults in mesenteric vessels; eggs in liver or feces), *Schistosoma japonicum* (Japan, China, Philippines; 600,000 sufferers; 25% of transmission due to animal reservoirs; mature adults in intestine or mesentery; eggs in spleen or liver), *Schistosoma haematobium* (Africa, Middle East; mature adults in bladder or mesentery; eggs in urine or liver), *Schistosoma mekongi* (only in Mekong River basin), *Schistosoma intercalatum* (worms and eggs in mesenteric portal system, vesical system not involved; mainly colonic and rectal involvement), *Schistosoma mattheei*

Diagnosis: bentonite flocculation test (1:5 titre diagnostic if cholesterol lecithin flocculation test also positive), complement fixation test, counterimmunoelectrophoresis, fluorescent antibody staining of serum, indirect hemagglutination titre, FAST-ELISA; light microscopy of stool (acid-ether concentrate), urine (concentrate; midday for *Schistosoma haematobium*), aspirate, puncture, unstained biopsy of rectum; anemia (erythrocyte count and hemoglobin decreased)

***Schistosoma japonicum* and *Schistosoma mekongi*:** urticarial rash and fever followed by dysentery, bloody and mucoid stools, epigastric pain, acute hepatitis, high eosinophilia, weight loss and hyperemia; may be liver cirrhosis, splenomegaly and ascites in late stage

***Schistosoma mansoni*:** pruritic papular rash followed by dysentery, bloody and mucoid stools, abdominal pain, nausea, vomiting, eosinophilia, hepatosplenomegaly or liver cirrhosis

***Schistosoma intercalatum*:** similar to, but milder than, *Schistosoma mansoni*

Schistosoma haematobium: microscopic and macroscopic hematuria, painful and frequent micturition; chronic sequelae hydronephrosis, renal failure and squamous cell carcinoma of bladder

Treatment:

***Schistosoma haematobium, Schistosoma mansoni*:** praziquantel 20 mg/kg orally for 2 doses after food 4 h apart

***Schistosoma japonicum, Schistosoma mekongi*:** praziquantel 20 mg/kg orally for 3 doses after food at 4 hourly intervals

Prevention and Control: mass chemotherapy; control of snails *Bulanus* (*Schistosoma haematobium*), *Biomphalaria* and *Oncomelicera* (*Schistosoma mansoni*, *Schistosoma japonicum*); controlled sanitation

KATAYAMA SYNDROME (ACUTE SCHISTOSOMIASIS

Agents: *Schistosoma mansoni* (primary and secondary), *Schistosoma japonicum* (primary and secondary), *Schistosoma haematobium* (primary; rare)

Diagnosis: fever, cough, hepatosplenomegaly, myalgias, urticaria, eosinophilia; pulmonary infiltration visible radiologically; at least 3X1g stool samples concentrated by modified Ritchie technique and examined for ova; ova in urine; immunofluorescent antibody tests on serum

Treatment: praziquantel as above + dexamethasone

CYSTICERCOSIS (CYSTICERCAL DISEASE, CYSTICERCIASIS, CYSTICERCOUS DISEASE, *TAENIA SOLIUM* CYSTICERSOSIS): eggs in food contaminated by infected person or autoinfection; areas of low socioeconomic development in Central and S Africa, Mexico (causes 1.9% of all human deaths), Central and S America, Southern Asia; subcutaneous tissues, skeletal muscles, brain, eye, heart, lungs, liver; presentation time may be delayed for up to 30 y, with mean presentation time being 5 y

Agent: *Taenia solium*; one case due to *Taenia crassiceps* reported

Diagnosis: subcutaneous or muscular disease often asymptomatic but subcutaneous nodules or intramuscular swellings occur; if larvae become lodged in vital organs, differing manifestations, according to site of disease and number of larvae, may result; cerebral cysticercosis frequently causes epileptiform fits; death may ensue; computed tomography of brain; X-ray of large muscle; hemagglutination of serum (≥ 1:128) and CSF (≥ 1:8), ELISA, enzyme-linked immunoelectrotransfer blot assay

(sensitivity 98%, specificity 100%), indirect fluorescent antibody titre; histology of biopsied nodules; 53% of patients have intestinal taeniasis

Posterior Fossa Syndrome: lymphocytosis, elevated protein level and diminished glucose level of CSF

Meningoencephalitis: eosinophilia of CSF

Treatment: praziquantel 50 mg/kg orally daily in 3 divided doses for 15 d + dexamethasone 12-16 mg orally daily or prednisone 30-40 mg orally daily in neurocysticercosis; albendazole; surgery for ventricular involvement and in cases of raised intracranial pressure

TRICHINELLOSIS (TRICHINA WORM INFECTION, TRICHINELLIASIS, TRICHINIASIS, TRICHUROSIS, TRICHINOUS MYOSITIS, TRICHINOUS POLYMYOSITIS)

Agents: *Trichinella spiralis*

Diagnosis: often asymptomatic; fever in 90% of cases, myalgias in 80%, periorbital edema in 75%, headache in 50%, urticarial rash in 20%, peripheral edema in 20%, intermittent diarrhoea in 15-51% (in early stages), nausea in 15%, subconjunctival hemorrhages in 10%, splinter hemorrhages in 10%, vomiting, abdominal discomfort, malaise, myositis, neurologic symptoms; cardiac, pulmonary or cerebral complications or toxemia may occur and can be fatal unless properly treated; unusual presentation of prolonged diarrhoea without fever and with brief muscle symptoms in Canadian Arctic (may affect 20% of Arctic population); worms and larvae in feces 7-14 d after ingestion; histology of cysts in muscle (quadriceps muscle biopsy positive in 91% of cases); ELISA, latex agglutination (screening test), immunodiffusion (if positive in latex agglutination), bentonite flocculation test (positive in 40% of cases; diagnostic titre 1:5), complement fixation test, indirect hemagglutination; neutrophilia with eosinophilia by tenth day, very high eosinophil count by 3-4 w, anemia (erythrocyte count and hemoglobin may be decreased)

Treatment: mebendazole in increasing doses to 600 mg orally 8 hourly for 30 d before surgical removal or in increasing doses to 200 mg/kg daily orally for 16-48 w in order to obtain serum levels > 100 mg/mL 1-3 h after an oral dose if inoperable; albendazole 10 mg/kg orally daily for 8 w

ECHINOCOCCOSIS (HYDATID CYST): wherever man comes into contact with canines in sheep-rearing countries; ≈ 30 notified cases/y in Australia (≈ 59% in Victoria); ≈ 3 deaths/y in USA; 40-66% of cysts in liver and peritoneum, 22-30% in lungs, 10% subcutaneous, 3% in female genital, 2% in spleen, 2% in bones, 2% in orbit, 2% in parotid glands and neck, 1-3% in kidneys, 1% in brain, 1% in breast

Agents: *Echinococcus granulosus*, *Echinococcus multilocularis, Echinococcus oligarthus*, *Echinococcus vogelsi*

Diagnosis: liver enlargement with palpable mass and 'hydatid thrill', hemoptysis, bone fracture, space-occupying lesion in brain; contact with dogs; peripheral eosinophilia; X-ray (calcification); liver scan; arteriography; ultrasound and computed tomographic imaging most reliable; identification of scolices, brood capsules or daughter cysts after surgical removal or autopsy or in aspirated fluid, or fragments from a ruptured cyst in sputum or urine (should be no attempt at aspiration on account of risk of spreading infection); cardiac hydatid cyst life threatening but rare; complement fixation test, indirect hemagglutination titre (> 1:320; highly specific but positive in only 51%; remains elevated for many years after infection), counterimmunoelectrophoresis (superior indicator of efficacy of treatment, as titres return to negative within 2 y of successful treatment), RAST (detects hydatid-specific IgE present in hepatic involvement but only in ≈ 25% of cases in which lung infected), bentonite flocculation test (1:5 titre diagnostic if indirect hemagglutination assay also positive), latex agglutination, indirect immunofluorescence, immunodiffusion, passive hemagglutination

***Echinococcus granulosus*:** clinical manifestations depend on number, size and location of cysts

***Echinococcus multilocularis*:** disease of liver resembles mucoid carcinoma, with hepatosplenomegaly, jaundice and ascites

Treatment: conservative, with local use of scolicide; aspiration of cavity, injection of 95% ethanol into cystic cavity and slow reaspiration; surgery when cyst producing symptoms or increasing in size or with cardiac cyst; albendazole 7.5 mg/kg to 400 mg orally 12 hourly (not < 6 y)

TOXOPLASMOSIS: worldwide; possibly commonest protozoal infection; 30% of adults in UK have antibodies; ≈ 200 cases (≈ 13 deaths)/y in USA; prevalence 20-100%; intrauterine infection (incidence 50% in women receiving initial infection in pregnancy) produces varying degrees of brain damage, myocarditis, retinochoroiditis and may cause miscarriage; infection in children and adults (principal modes of infection accidental ingestion of oocysts in rare to medium beef, while working in an outside garden or on exposure to cats; also in meat handlers through skin abrasions; other accidental routes of transmission include blood transfusion, laboratories, organ transplantation and autopsies; recent outbreak due to contaminated municipal water reported) may produce no symptoms, fever, mild off-colour feeling, hepatitis-like syndrome, mononucleosis-like syndrome, myocarditis, typhus-like syndrome, atypical pneumonia, lymphadenopathy (27.5% of cases), retinochoroiditis (60% of cases), acute meningoencephalitis (rare; may be terminal in Hodgkin's disease, in leukemia, after irradiation and after immunosuppressive drugs), chronic infection with cysts persisting in CNS, heart, skeleton and smooth muscle

Agent: *Toxoplasma gondii*

Diagnosis:

Acquired Toxoplasmosis: usually asymptomatic or mild and self-limiting; 20% cervical or generalised lymphadenopathy and/or a flu-like illness; overt disease (disseminated toxoplasmosis) relatively rare, characterised by abrupt onset, prolonged remittent fever, maculopapular rash, chorioretinitis, uveitis, internal hydrocephalus, delirium and convulsions; myocarditis or pneumonitis often seen; may be rapidly fatal in persons with impaired immune response (especially those undergoing immunosuppressive therapy and those with AIDS (6.2% of opportunistic infection in AIDS), pediatric heart transplant recipients, lymphoma, leukemia; from accidental ingestion of contaminated substances (eg., in gardening or cleaning cat litter box) or from raw or partly cooked beef, pork, lamb or venison; light microscopy of aspirate, puncture, biopsy of lymph node; Giemsa-stained smear of bronchoalveolar lavage; isolation from blood or other body fluids; serology generally reliable, although status of disease activity may be unclear—indirect fluorescent antibody test (IgG onset to rise 0-2 mo, duration years, rising titre in acute disease, titre present in ocular disease, stable or rising titre in congenital disease in neonate, false positives and negatives; IgM indicates recent infection, onset to rise 0-1 mo, duration 3 w - 18 mo, titre present in acute disease, false positives in patients with anti-nuclear antibodies), latex agglutination (IgG and IgM antibodies), differential agglutination (IgG; differentiates recent infection from remote in adults and older children), complement fixation test (onset to rise 1-5 mo, duration years; rising titre in acute disease, titre present in ocular disease, stable or rising titres in congenital disease in neonate), direct immunofluorescence, ELISA (antibody; IgG, (appears in 1-2 w, peaks at 6-8 w, declines but may persist for life), IgM (appears early and may persist 1 or more years; negative results in immunocompetent usually excludes infection but positive not useful in adults), IgM capture, IgA (positive in infected adults and congenitally infected infants; may persist for months or years; avidity assay useful in first trimester), IgE (presence in adults usually indicates acute infection; present in congenital infection; absence does not exclude infection)), indirect hemagglutination titre (onset to rise 2-5 mo, duration years, rising titre in acute disease, stable or rising titre in congenital disease in neonate; antibodies found in > 1/3 of population), Sabin-Feldman dye test (IgG; onset to rise 0-2 mo, duration years; mainly reference laboratories; negative result practically rules out prior exposure), IgG avidity (urea dissociable; low avidity indicates primary infection), IgE immunosorbent assay; histopathology of enlarged lymph node; mouse inoculation; anemia (erythrocyte count and hemoglobin may be decreased), atypical monocytes

Congenital Toxoplasmosis: many cases asymptomatic but may be severe, with fever, jaundice, rash and hepatosplenomegaly, and complicated by chorioretinitis, encephalitis, hydrocephalus, microcephaly, convulsions, mental retardation, cerebral calcification and cerebral palsy; some signs and symptoms may develop several years after birth; positive IgM and low avidity test in mother at 3-4 mo; isolation from placenta, umbilical cord or infant blood; PCR of white blood cells, CSF or amniotic fluid (reference laboratory)

Toxoplasmosis of Brain: recent onset of a focal neurologic abnormality consistent with intracranial disease or a reduced level of consciousness + evidence by brain imaging (computed tomography or nuclear magnetic resonance) of a lesion having a mass effect or the radiographic appearance of which is enhanced by injection of contrast medium + serum antibodies to toxoplasmin or successful response to therapy for toxoplasmosis

Treatment: sulphadiazine 50 mg/kg to 1-1.5 g orally or i.v. 6 hourly for 3-6 w (clindamycin 600 mg orally or i.v. 6 hourly if hypersensitive) + pyrimethamine 50-100 mg (child: 2 mg/kg to maximum 25 mg) orally first dose then 25-50 mg orally daily (child: 1 mg/kg daily; infant: every second or third day) for 3-6 w + folinic acid 3-9 mg orally daily; in AIDS, followed by sulphadiazine 500 mg orally 6 hourly (clindamycin 600 mg orally 8 hourly if hypersensitive) + pyrimethamine 25-50 mg orally daily + folinic acid; spiramycin 50-100 mg/kg to 2-4 g orally daily for 4 w, cotrimoxazole 160/800 mg (child: 1.5/7.5 mg/kg) twice daily for 4 w; azithromycin + pyrimethamine

Pregnancy: spiramycin 3 g daily in divided doses throughout pregnancy

Prophylaxis in AIDS: cotrimoxazole 80/400-160/800 mg orally daily or 160/800 mg orally 3 times weekly, dapsone 100 mg orally 3 times a week ± pyrimethamine, atovaquone + pyrimethamine, pyrimethamine alone, azithromycin, clarithromycin

STRONGYLOIDIASIS: tropical and temperate areas; 42% gastrointestinal disturbance (diarrhoea, malabsorption, abdominal pain, bloating, weight loss), 25% asymptomatic, 22% skin complaints (transient serpiginous urticaria, weals on waist and buttocks, persistent rash), 7% pruritus ani, 4% fever; eosinophilic pneumonia due to larval migration through lung; eosinophilia (83% > 400 eosinophils/μL); severe strongyloidiasis in immunocompromised: 66% hyperinfection (50-86% mortality), 21% disseminated (71% mortality), 15% intestinal (20% mortality), may lead to bacteremia and meningitis with enteric organisms; asymptomatic individuals from at-risk populations (immigrants, refugees, war veterans who have served in tropics, requiring corticosteroids and possibly exposed to *Strongyloides*), patients with eosinophilia and history of possible exposure, and patients with suggestive abdominal symptoms or skin manifestations should be tested

Agents: *Strongyloides stercoralis*, *Strongyloides fuelleborni*

Diagnosis: microscopy for larvae and ova in feces 3 or more concentrated specimens); Harada-Mori or agar plate culture; ELISA (IgG to *Strongyloides ratti*; 84-95% sensitivity; does not distinguish between current and past infection); indirect fluorescent antibody titre in patients with long-standing symptoms

Severe Strongyloidiasis: fever in 71% of cases, abdominal pain in 66%, dyspnoea in 56%; diffuse alveolar infiltrates in 56%; isolation of larvae from stool in 59%, sputum in 38%, lung and duodenum at autopsy in 18%

Treatment and Prophylaxis: ivermectin 200 μg/kg/d on days 1, 2, 15, 16; albendazole 400 mg once orally on 3 consecutive days

DISSEMINATED MICROSPORIDIOSIS: HIV, renal transplant recipients

Agent: *Encephalitozoon cuniculi*

Diagnosis: chromotrope-based stains of urine, stools, sputum, conjunctival scrapings; electron microscopy, immunofluorescence, polymerase chain reaction, cultures of affected tissue

Treatment: oral albendazole, topical fumagillin, withdrawal of immunosuppressive therapy

INTERNAL HIRUDINIASIS: leeches enter and attach themselves to mucous membrane of upper respiratory tract, digestive passage or genitourinary tract

Agents: *Limnatis nilotica* and other *Limnatis* species

Diagnosis: hemoptysis, hematemesis, severe anemia, occasionally death from excessive loss of blood; suffocation may occur in laryngeal or tracheal hirudinasis ('halzoun') caused by *Limnatis nilotica*; history of drinking or bathing in leech-infested water

Treatment: removal if possible

LINGUATULOSIS (LINGUATULIASIS): uncommon disease in which intestine, lung, nasopharyngeal region, eye (with visual damage) or other organs may be affected

Agent: '*Linguatula serrata*'

Diagnosis: direct visualisation

Treatment: removal if possible

SYSTEMIC INFECTIONS IN IMMUNOCOMPROMISED

Diagnosis: blood cultures; examination and culture of CSF, sputum culture, other investigations as indicated

Agammaglobulinemia

Agents: *human echovirus*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*

Treatment: β-lactamase-resistant cephalosporin

Prophylaxis: amoxycillin, cotrimoxazole, tetracycline, IgG (passive immunisation)

Cell-mediated Immune Disorders

Agents: fungi, *Simplexvirus*, *Legionella*, *Listeria*, *Mycobacterium*, *Nocardia*, *Pneumocystis jiroveci*, *Toxoplasma*

Treatment: dependent on clinical and laboratory evaluation

Prophylaxis: cotrimoxazole, nystatin, interferon, interleukin 2, thymic hormones, transfer factor

Chemotactic Defect

Agents: *Candida*, *Cryptococcus*, *Haemophilus influenzae*, *Staphylococcus aureus*

Treatment: antistaphylococcal drug

Complement Deficiency:

C1, 2, 3, 4, Factor B

Agents: aerobic Gram negative bacilli, *Haemophilus influenzae*, *Neisseria meningitidis*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*

Treatment: β-lactamase-resistant cephalosporin

Prophylaxis: plasma

C5, 6, 7, 8

Agents: *Neisseria gonorrhoeae*, *Neisseria meningitidis*

Treatment: benzylpenicillin

Prophylaxis: plasma

Granulocytopenia

Agents: *Aspergillus*, *Candida*, *Corynebacterium*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, coagulase negative staphylococci

Treatment: aminoglycoside + antipseudomonal penicillin, ciprofloxacin + piperacillin

Breakthrough Bacteremia: if isolate Gram positive, add vancomycin; if isolate Gram negative, switch to new regimen

Catheter-associated Infection: add vancomycin

Severe Oral Mucositis or Necrotising Gingivitis: add clindamycin or metronidazole

Esophagitis: institute trial of oral clotrimazole or ketoconazole or i.v. amphotericin B 0.5 mg/kg/d

Diffuse or Interstitial Pneumonitis: institute trial of cotrimoxazole and erythromycin (continue initial antimicrobials if granulocytopenic)

New Pulmonary Infiltrate: if granulocyte count rising, watch and wait; if granulocyte count not recovering, perform biopsy to establish diagnosis; if biopsy cannot be done, add amphotericin B 0.5 mg/kg/d empirically

Perianal Tenderness: add clindamycin or metronidazole

Persistent Fever and Neutropenia: continue antibacterials; if fever and neutropenia persist for a week, add systemic antifungal therapy empirically

Prophylaxis: cotrimoxazole, nystatin, granulocyte transfusions, passive immunisation, plasma

Hyposplenism/Splenectomy

Agents: *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*

Treatment: β-lactamase-resistant cephalosporin

Prophylaxis: penicillin, pneumococcal vaccine, '*Corynebacterium parvum*'

Microbicidal Abnormality

Agents: *Aspergillus*, *Candida*, *Pseudomonas*, *Serratia*, *Staphylococcus aureus*

Treatment: antistaphylococcal drug + cotrimoxazole

Chapter 15

Fever of Undetermined Origin (Pyrexia of Unknown Origin)

0.5% of new episodes of illness in UK; 0.2% of ambulatory care visits in USA

Agents: multisystem/collagen vascular disease (19% total, 30% in elderly, 17% in children; juvenile rheumatoid arthritis, serum sickness, vasculitis, drug fever, systemic lupus erythematosus, erythema multiforme, rheumatic fever, mixed connective tissue disease infection, granulomatous hepatitis, temporal arteritis, sarcoidosis), neoplasm (28% total, 2% in children; Hodgkin's disease, non-Hodgkin's lymphoma, leukemia, preleukemia, aleukemia, hypernephroma, hepatoma, atrial myxoma), infection (11% total, 30% in elderly, 17% in children; tuberculosis, infectious endocarditis, intraabdominal and intraperitoneal abscesses, osteomyelitis, urinary tract infections, biliary tract infections; uncommonly, Q fever, brucellosis, salmonellosis, toxoplasmosis, disseminated mycosis, chronic meningococcemia, psittacosis, relapsing fever, typhus, lymphogranuloma venereum, *human cytomegalovirus*, *Epstein-Barr virus*), miscellaneous causes (regional enteritis, factitious fever, exaggerated circadian temperature variation, pulmonary embolism, alcoholic hepatitis, familial Mediterranean fever, Whipple's disease, periodic fever, CNS lesion), no diagnosis (5% in adults, 16% in children)

Diagnosis: fever for at least 21 d, oral temperature of 38.3°C or greater on several occasions, no established diagnosis after 1 w of clinical investigation; white cell count (leucopenia in miliary tuberculosis, brucellosis, lymphoma, systemic lupus erythematosus) and differential (monocytosis in bacterial endocarditis, tuberculosis, brucellosis, solid tumour, Hodgkin's disease, inflammatory bowel disease; lymphocytosis in tuberculosis, infectious mononucleosis, *human cytomegalovirus* infection), direct examination of blood, erythrocyte sedimentation rate (elevated in subacute bacterial endocarditis, lymphoma, giant cell arteritis, rheumatic fever, Still's disease), alkaline phosphatase (elevated in subacute thyroiditis, obstructive or infiltrative disease of the liver, hypernephroma, Still's disease, Hodgkin's disease, giant cell arteritis) and other liver function tests (SGOT), ASOT, rheumatoid factor (positive in subacute bacterial endocarditis), antinuclear antibody test, serum uric acid, calcium and phosphorous, urinalysis, stool guiac; chest X-ray, multiple blood cultures, skin tests, gastrointestinal X-rays, intravenous pyelogram and renal ultrasound, liver/spleen scan and ultrasound, echocardiography, abdominal computerised axial tomography scan, ultrasound or gallium scan, ventilation/perfusion lung scan, acute and convalescent sera for Q fever, *human cytomegalovirus*, toxoplasmosis, brucellosis, trichinosis, psittacosis and infectious mononucleosis, lumbar puncture, bone survey or scan, panorex of mandible; pulmonary angiography, celiac axis angiography, liver biopsy, bone marrow biopsy, lymph node biopsy, temporal artery biopsy, exploratory laparotomy (only if there is objective clinical evidence of abdominal disease); therapeutic trial with steroids if giant cell arteritis suspected, salicylates if Still's disease or rheumatic fever, antimicrobials if tuberculosis or infective endocarditis

Factitious Fever: lack of normal diurnal variation of temperature, extreme pyrexia (≥ 42°C), normal examination and laboratory data, temperature-pulse dissociation, recovery of multiple or unusual organisms in blood culture, lack of ill appearance of patient

Treatment: dependent on cause

YOUNG CHILDREN: most self-resolving viral illness but 7-13% occult bacteremia and serious bacterial infection

Agents: bacterial gastroenteritis, cellulitis, meningitis, osteomyelitis, pneumonia, septic arthritis, urinary tract infection

< 29 d or appears toxic:

Diagnosis: complete blood count with manual differential; blood cultures; lumbar puncture for cell counts, glucose, protein and culture; urinalysis and culture; tests for *human herpesvirus 1* if maternal infection at time of delivery, use of fetal scalp electrodes, vaginal delivery, cerebrospinal fluid pleocytosis, skin, eye or mouth lesions

Treatment: i.v. antibiotics; anti-herpes antiviral where indicated

29-90 d non-toxic:

Diagnosis: complete blood count with manual differential, urinalysis and culture ± cerebrospinal fluid analysis

Treatment: ceftriaxone 50 mg/kg i.m. may be given

3-36 mo: observation with close follow-up

Part 2: Organisms

Chapter 16

Viruses

Deltavirus: hepatitis D (Delta) Virus; RNA satellite virus; transmitted parenterally with hepatitis B virus; requires HBV to grow; causes hepatitis, liver cancer; chronicity; serum autoantibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced

dsDNA Viruses No RNA Stage

Adenoviridae: linear double strand DNA, molecular weight 20-30X10^6 D, 32-35 kb/strand, icosahedral ether-resistant (absence of lipids) capsid with 252 polygonal capsomeres, 60-90 nm diameter, 12 fibres, 4 minor proteins; penetrate host cells by endocytosis; replicate in nucleus of infected cells, producing basophilic inclusions; marked tendency to cause latent infection of tissues such as tonsils and adenoids; several serotypes (notably 12, 18, 31) oncogenic in hamsters and cell cultures; some serotypes agglutinate rat or rhesus erythrocytes; type-specific antibody can be measured by hemagglutination inhibition; related by family cross-reacting soluble antigens (except chicken adenovirus); transfection of cell by adenovirus requires only part of viral genome; important antigens for neutralisation proteins of capsid; proteins: hexon protein (type-specific and family cross reactions, no known biological activity, no hemagglutination, molecular weight 315,000 D, 105,000 polypeptide chains), complete protein (family cross reactive, cytopathic, attachment of virions to cells, partial hemagglutination, molecular weight 419,000), base protein (family cross reactive, cytopathic, no hemagglutination, molecular weight 236,000, 80,000 polypeptide chains), fibre protein (type specific, blocks synthesis of macromolecules, inhibits viral multiplication, partial hemagglutination, molecular weight 83,000), internal proteins (probably act in assembly of viral DNA, no hemagglutination, 19,000-55,000 polypeptide chains); diagnosis: isolation primary method, antigen detection described but not generally available, paired sera required for serology

Mastadenovirus: human adenoviruses; 49 serotypes/species; does not have a conventional envelope, but viral antigens appear on surface of infected cells, which are then susceptible to immune lysis; 252 capsomeres; survives 50 d in water (source animal and human feces); causes acute respiratory illness (serotypes 1-7, *human adenovirus 11, 14, 21*; upper and lower respiratory infection; mainly in children and military recruits; rhinitis, febrile catarrh (serotypes 3, 4, 7, *human adenovirus 14*), 'influenza-like illness', pharyngitis/sore throat (serotypes 1, 2, 3, 5, 6, 7, 16 (0.08% of all cases), *human adenovirus 21*), acute exudative tonsillitis (serotypes 1-7, *human adenovirus 14*), acute laryngitis, laryngotracheitis, tracheobronchitis (serotypes 1-5, 7), bronchitis, croup, pneumonia (serotypes 1, 2, 3, 5, 7), pneumonitis), pharyngoconjunctival fever (serotypes 3, 4, 7 *human adenovirus 14*), acute hemorrhagic conjunctivitis (*human adenovirus 11*), follicular conjunctivitis (serotypes 1-10, 16, *human adenvovirus 17, 19, 37*), keratoconjunctivitis (serotypes 7, 8, 18, *human adenovirus 19*), alimentary infection (gastroenteritis, acute diarrhoea and/or vomiting; < 4 y; epidemic; serotypes 40, 41, others in AIDS; 15% of nosocomial diarrhoea), arthritis, carditis, myocarditis and pericarditis, acute hemorrhagic cystitis in immunosuppressed (*human adenovirus 11*), 6% of encephalitis (especially serotype 7), non-pyogenic meningitis (15% of cases), hepatitis, intussusception, mesenteric lymphadenitis, maculopapular rash, roseola-like illness, rhabdomyolysis; increased infectiveness in abnormal host (clinical, subclinical and persistent nonlatent infections; T helper lymphocyte dysfunction); attaches to susceptible tissue cell by reaction of viral capsid protein with specific receptor on cell; replicates in intestinal tract, producing diarrhoea; enters across epithelial surface of intestinal tract and subsequently spreads through body; infects lymphocytes; persists in lymphoid tissue (non-infectious, shed to exterior); 80% of cases show transient appearance of autoantibodies to DNA; serum autoantibodies against cytoskeleton, myosin, myoglobin, thyroglobin, transferrin and heart muscle (in acute myocarditis only) also produced; immunity due to antibody (+), cell-mediated immunity (+); 23 genes; subgroup I (serotypes 3, 7, 11, 14, 16, 20, 21, 25, 28) agglutinate rhesus erythrocytes and have moderate oncogenic potential, viral DNA 12.5-13.7% of virion, molecular weight 23X10^6 D (35 kbp), 49-52% G+C, penton dodecagons; subgroup II (serotypes 8, 9, 10, 13, 15, 17, 19, 22, 23, 24, 26, 27) agglutinate rat erythrocytes and have low oncogenic potential, viral DNA 12.5-13.7% of virion, molecular weight 23-25X10^6 D (35-38 kbp), 57-61% G+C, penton dodecagons; subgroup III (serotypes 1, 2, 4, 5, 6) partially agglutinate rat, but not rhesus, erythrocytes and have low oncogenic potential, viral DNA 12.5-13.7% of virion, molecular weight ≈ 23X10^6 D (35kbp), 57-59% G+C, no penton dodecagons; subgroup IV (serotypes 12, 18, 31) do not agglutinate erythrocytes and have high oncogenic potential, viral DNA 11.6-12.5% of virion, molecular weight ≈ 21X10^6 D (30 kbp), 48-49% G+C, no penton dodecagons; growth in primary monkey kidney cells +++, human diploid fibroblasts +, Hep2 +++ (6 d to isolation, enlarged, clustered cells like bunches of grapes or lattice; verified by neutralisation test, fluorescent antibody, complement fixation test); diagnosis: complement fixation test, hemagglutination inhibition assay, neutralisation antibody titre, viral isolation from throat swab, conjunctival swab, pharyngeal washing, feces, CSF

Human adenovirus A

Serotype 18: causes epidemic keratoconjunctivitis

Human adenovirus B

Serotpye 3: causes acute respiratory illness, follicular conjunctivitis, coryza, epidemic keratoconjunctivitis, febrile catarrh, pharyngitis, acute exudative tonsillitis, tracheobronchitis, pneumonia with exanthema, pharyngoconjunctival fever, encephalitis; cough and fever in all adult cases and 97% of cases in children, diarrhoea in 45% of cases in children and 25% of adult cases, of cases in adults but not in children, vomiting in 26% of cases in children; chest X-ray infiltrates in all cases (bilateral in 66% of children and 33% of adults; $\geq$ 2 lobes or segments in 79% of children and 17% of adults); adenopathy in 50%, nausea in 48-77%, headache in 33-70%, conjunctivitis in 33%, myalgia in 33% and rhinorrhoea/rhinitis in 30-75% of adult cases but none of these in cases in children; dyspnoea in 55%, heart failure in 48%, meningismus in 38% and deaths in 10% of cases in children but none of these in adult cases

Serotype 7: causes acute respiratory illness, follicular conjunctivitis, coryza, epidemic keratoconjunctivitis, febrile catarrh, pharyngitis, acute exudative tonsillitis, tracheobronchitis, pneumonia with exanthema, pharyngoconjunctival fever, encephalitis

Human adenovirus 11: causes acute respiratory illness, acute hemorrhagic conjunctivitis, acute hemorrhagic cystitis

Human adenovirus 14: causes acute respiratory illness, febrile catarrh, coryza, acute exudative tonsillitis, pharyngitis, pharyngoconjunctival fever

Serotype 16: causes follicular conjunctivitis (in 50% of infections), acute exudative tonsillitis (0.08% of all cases), pharyngitis

Human adenovirus 21: causes acute respiratory illness, acute hemorrhagic cystitis

Human adenovirus 37: causes acute respiratory illness, follicular conjunctivitis, coryza, epidemic keratoconjunctivitis, febrile catarrh, pharyngitis, acute exudative tonsillitis, tracheobronchitis, pneumonia with exanthema, pharyngoconjunctival fever, encephalitis; cough and fever in all adult cases and 97% of cases in children, diarrhoea in 45% of cases in children and 25% of adult cases, of cases in adults but not in children, vomiting in 26% of cases in children; chest X-ray infiltrates in all cases (bilateral in 66% of children and 33% of adults; $\geq$ 2 lobes or segments in 79% of children and 17% of adults); adenopathy in 50%, nausea in 48-77%, headache in 33-70%, conjunctivitis in 33%, myalgia in 33% and rhinorrhoea/rhinitis in 30-75% of adult cases but none of these in cases in children; dyspnoea in 55%, heart failure in 48%, meningismus in 38% and deaths in 10% of cases in children but none of these in adult cases;

Human adenovirus 50

Human adenovirus C

Serotye 1: causes acute respiratory illness, follicular conjunctivitis, pharyngitis, pharyngoconjunctival fever, acute exudative tonsillitis, tracheobronchitis, pneumonia

Serotype 2: causes acute respiratory illness, follicular conjunctivitis, pharyngitis, pharyngoconjunctival fever, acute exudative tonsillitis, tracheobronchitis, pneumonia, left ventricular dysfunction

Serotype 5: causes acute respiratory illness, follicular conjunctivitis, pharyngitis, pharyngoconjunctival fever, acute exudative tonsillitis, tracheobronchitis, pneumonia

Serotype 6: Causes acute respiratory illness, follicular conjunctivitis, pharyngitis, acute exudative tonsillitis

Human adenovirus D

Serotype 8: causes epidemic keratoconjunctivitis, nonpurulent conjunctivitis

Serotype 9: causes follicular conjunctivitis

Human adenovirus 10: causes follicular conjunctivitis

Serotype 17: causes nonpurulent conjunctivitis

Human adenovirus 19: causes epidemic keratoconjunctivitis, nonpurulent conjunctivitis

Human adenovirus 20

Human adenovirus 28

Human adenovirus 37: causes cervicitis (sexually transmitted), nonpurulent conjunctivitis

Human adenovirus E

Serotype 4: causes acute respiratory illness, febrile catarrh, coryza, acute exudative tonsillitis, pharyngitis/sore throat, pharyngoconjunctival fever, nonpurulent conjunctivitis (in 68% of infections), arthritis (in 8% of infections); fever in 89%, systemic symptoms in 78%, pharyngitis in 56%, tracheobronchitis in 44%, rhinorrhoea/rhinitis in 44%, chest X-ray infiltrates in 22% of adult cases

Human adenovirus F

Serotype 40: causes gastroenteritis

Serotype 41: causes gastroenteritis

Order Herpesvirales

Family Herpesviridae: double strand DNA; molecular weight 54-102X10^6 D in icosahedral capsid 100 nm diameter with 162 hollow capsomeres surrounded by lipid envelope of host cell origin, 180-250 nm diameter; ether and chloroform sensitive; replicate in nucleus of infected cells (biosynthesis of viral DNA and assembly of viral particles) and acquire outer envelope

from infected cell on passage through nuclear membrane; multiply in macrophages; 100 genes; latency (restricted or altered gene expression gives absence of immunogenic proteins, persist in presence of antibodies) and oncogenicity; eosinophilic intranuclear inclusions (Cowdry type A) in infected cells; some species multiply on a variety of cultured cells; antibodies provide some protection against certain strains; infections produce solid immunity; penetrate cells by fusion; no common family antigen

Subfamily Alphaherpesvirinae

Simplexvirus: molecular weight $100X10^6$ D, 151 kb/strand, 100 nm, 162 capsomeres, virion 180-200 nm; causes latent infection, grows rapidly in vitro, causes symptomatic reactions by axonal spread from infected ganglion; increased infectiousness in abnormal host (clinical and latent infections); genital sites: 86% *human herpesvirus 2*, 14% *human herpesvirus 1*; orofacial sites: 96% *human herpesvirus 1*, 4% *human herpesvirus 2*; finger/hand: 54% *human herpesvirus 1*, 46% *human herpesvirus 2*; other non-genital sites: 60% *human herpesvirus 1*, 40% *human herpesvirus 2*; carried in blood associated with mononuclear cells; inhibits phagocytic (macrophage) chemotaxis and secretory function; persistence due to failure to display viral antigen on infected cell surface, residence in cells (eg., neurons) that do not express major histocompatibility antigens prevents T cell recognition; IgG antibodies nonspecifically bind to infected cell and block immune lysis; virally encoded F_c receptor inhibits classical complement pathway; virally encoded complement receptor inhibits alternative complement pathway; antibody binding to surface of virus-containing cell may inhibit viral replication and allow virus to persist; in vitro T cell suppressors; tunicamycin-sensitive viral glycoprotein induces immunosuppression by direct inhibition of lytic activity of natural killer cells; recovery from primary infection due to cell-mediated immunity (delayed type hyperactivity type activated macrophage +++, direct cytotoxicity +++), neutralising antibody (++), antibody-initiated, complement-dependent lysis requiring antiviral IgG and alternative pathway of complement (++); ? resistance to reactivation of latent infection due to antibody; persists in dorsal root ganglia (non-infectious, shed to exterior; activation causes cold sore) and salivary gland (infectious and shed to exterior); diagnosis: isolation in tissue culture (MRC-5 shell vial centrifugation enhancement best method; material from vesicle fluid, throat swab, CSF, corneal scraping; WI38, primary monkey kidney ++, human diploid fibroblasts +++, Hep2 ++, embryonated egg; 3-4 d to isolation, enlarged or shrunken granular cells starting at edge, rapid progression and sloughing, may have giant cells; verified by fluorescent antigen, ELISA; sensitivity 50% for primary, 20% for recurrent), HerpesSelect kit for IgG antibody (*human herpesvirus 1* and *2*; 50% +ve at 3 w, 98% at 6 w), POCkit for *human herpesvirus 2* antibody (positive in few weeks), antigen detection (direct immunoperoxidase staining) variably adequate, Tzanck smear, electron microscopy; treatment: aciclovir, valaciclovir, famciclovir, penciclovir, idoxuridine, vidarabine

Human herpesvirus 1: causes anterior uveitis, arthritis, non-purulent conjunctivitis (uncommon), disseminated infection associated with atopic eczema in children (exogenous), dysuria without frequency, 12-21% of encephalitis (all ages; peak incidence > 30 y old; endogenous or exogenous; temporal lobe), perinatal and prenatal generalised disease (exogenous), acute herpetic gingivostomatitis (< 15 y; peak incidence 1-4 y; exogenous), adult (associated with pregnancy, thymic dysplasia, celiac disease, corticosteroid therapy, leukemias and lymphomas, severe burns, renal transplantation, AIDS), neonatal and prenatal hepatitis, infections in abnormal host (T helper lymphocyte dysfunction), iritis, keratoconjunctivitis (> 1 y; peak incidence > 3 y), localised skin lesions (Kaposi's varicelliform eruption all ages, peak incidence > 15 y; herpes febrilis ('cold sores') type 1, > 4 y, peak incidence > 30 y, endogenous), meningoencephalitis, papulovesicular rash (neonatal), esophagitis, proctitis, rhabdomyolysis, acute exudative tonsillitis, acute chest infection, pneumonia (neonatal and diffuse interstitial in T cell deficiency) with exanthem, urinary infections, whitlow, systemic infections in cell-mediated immunity disorders; generally decreased incidence but increased proportion of genital; transmitted by droplets, saliva;

Human herpesvirus 2: causes balanitis, non-purulent cervicitis, encephalitis, perinatal and prenatal generalised disease (exogenous), genital herpes (sexually transmitted; very common (globally, 536 million aged 15-49 infected, with 23.6 million new infections/y; reactivates; > 14 y; peak incidence 15-29 y; primary exogenous, recurrent endogenous), urethritis, vaginitis, vulvitis, 4-10% of non-pyogenic meningitis (exogenous; common in impaired cell-mediated immunity), ? cervical carcinoma co-factor, ? psychosis associated with in utero exposure; increased incidence, lower incidence of primary disease but higher incidence of recurrent disease in higher socioeconomic groups; enters across epithelial surface of urinogenital tract and subsequently spreads through body (> 90% of persons with genital HSV-2 shed virus asymptomatically; 60% of infections unrecognised with symptoms, 20% recognised genital herpes, 20% truly asymptomatic)

***Cercopithecine herpesvirus*:** herpes simiae; causes encephalitis

Varicellovirus

Human herpesvirus 3: varicella-zoster virus; causes varicella (chickenpox), zoster (shingles), abortion, anterior uveitis, arthritis, non-purulent conjunctivitis, 3% of encephalitis, Guillain-Barré syndrome, adult, pediatric and prenatal hepatitis, iridocyclitis, iritis, keratoconjunctivitis, non-pyogenic meningitis (common in impaired cell-mediated immunity), mouth lesions, myocarditis and pericarditis, oophoritis, pneumonia (including diffuse interstitial) with exanthem, pneumonitis, prenatal generalised disease, 5-30% of Reye's syndrome, vesicular rash, systemic infections in cell-mediated immunity disorders; increased infectiousness in abnormal host (clinical and latent infections; T helper lymphocyte dysfunction); infects lymphocytes; residence in cells (eg., neurons) that do not express major histocompatibility agents prevents T cell recognition;

virally encoded F_c receptor inhibits classical complement pathways; primary bodily defence mechanism cellular immune responses (delayed type hypersensitivity activated macrophage +++, direct cytotoxicity +++), neutralising antibody (++); recovery from primary infection and resistance to reactivation of latent infection due to cell-mediated immunity (+++); persists in dorsal root ganglia (non-infectious, shed to exterior), activation producing zoster; serum autoantibodies against cytoskeleton and insulin produced; diagnosis: serology (complement fixation test, hemagglutination inhibition, indirect fluorescent antibody titre, ELISA, radioimmunoassay) not useful except for immune status, isolation in tissue culture (scrapings from skin lesions, vesicle fluid, sputum; WI38, primary monkey kidney +, human diploid fibroblasts ++, not Hep2) primary method (6-8 d to isolation; discrete, elongated foci of enlarged or shrunken cells, slow contiguous progression, enhanced by use of growth medium; verified by cell association, hematoxylin and eosin, fluorescent antigen, complement fixation test), electron microscopy, Tzanck smear, antigen detection useful; treatment: aciclovir

Subfamily Betaherpesvirinae

Human cytomegalovirus: human herpesvirus 5; may have basophilic inclusion bodies; latent infection; prevalence of antibody in adults varies from 40% in France to 100% in Manila and Uganda; causes abortion, arthritis, cytomegalic inclusion disease, perinatal, prenatal and postnatal generalised disease, adult, neonatal and prenatal hepatitis, mononucleosis, pneumonia and pneumonitis, stillbirth, teratogenic effects, Guillain-Barrè syndrome, prenatal urinary infection; increased infectiousness in abnormal host (clinical, subclinical, latent and persistent nonlatent infections); causes retinochoroiditis, conjunctivitis, acute diarrhoea and/or vomiting, colitis, pancreatitis (59% of cases), encephalitis, myelitis, myocarditis and pericarditis, stomatitis, esophagitis, gastritis, antral obstruction, cholecystitis/cholangitis/papillary stenosis, hepatic granuloma, hepatitis, ileitis/colitis, otitis media, proctitis, pneumonia, adrenalitis, epididymitis, cervicitis in AIDS; also extremely infrequent encephalitis in impaired cell-mediated immunity, diffuse interstitial pneumonia in allogenic bone marrow transplant recipients, infusion infections, and other infections in T lymphocyte dysfunction), ? atherosclerosis; virus presence in semen and cervix suggests sexual transmission; carried in blood associated with mononuclear cells; infects lymphocytes, affecting functions of T, B, NK cells and macrophages (accessory function, interleukin 2, suppressor activity), decreases polymorphonuclear bactericidal and chemotactic functions, but usually a secondary agent, though evidence that assists HIV infection; virally encoded F_c receptor inhibits classical complement pathways; down-regulation of major histocompatibility class I antigens prevents $CD8^+$ T cell recognition; selective interference of viral antigen processing by another viral protein (eg., protease inhibitors) prevents T cell recognition; virally encoded protein homologous to cellular G protein coupled receptors inhibits inflammatory cell formation; persistent infection of glands, etc, inaccessible to circulating antibody; IgG antibodies nonspecifically bind to infected cell and block immune lysis; primary bodily defence mechanism cellular immune responses (delayed type hypersensitivity activated macrophage ++, direct cytotoxicity +++), neutralising antibody (++), basophil-mast cell (+); recovery from primary infection and resistance to reactivation of latent infection due to cell-mediated immunity; persists in lymphoid tissue (non-infectious, shed to exterior), activation ± disease occurring; *human cytomegalovirus* is a polyclonal B cell activator and triggers B lymphocytes with a broad range of specificities; autoantibodies are common (DNA, erythrocytes, lymphocytes, neutrophils, platelets, immunoglobulin, cytoskeleton, smooth muscle, thyroglobulin); diagnosis: serology (IgM: indirect fluorescent antibody titre, complement fixation test, neutralisation test, ELISA (IgG, IgM, IgM capture); IgG seroconversion or presence of specific IgM useful in nonimmunocomprised), isolation in tissue culture (primary method and only useful method in kidney and liver transplant recipients; human diploid fibroblasts ++, no growth in primary monkey kidney or Hep2; 6-10 d to isolation, compact foci of enlarged cells, slow contiguous progression; verified by cell association, fluorescent antigen, haematoxylin and eosin; first morning's sample of urine most dependable source but may reflect remote infection; also heparinised blood during acute phase and throat swabs; may be cultured from asymptomatic persons—saliva (mostly children), rarely from blood, 1% of normal semen specimens, breast milk specimens in 25% of seropositive women, cervical secretions in 15% of first trimester pregnancies), demonstration of viral antigen or DNA/RNA in diseased lung, oesophagus, colon or blood (may be only useful method in immunocompromised); treatment: ganciclovir or foscarnet + i.v. immunoglobulin

Roseolovirus

Human herpesvirus 6: causes exanthema rubitum (roseola, 'sixth disease') and pneumonitis in infants, disease resembling acute infectious mononucleosis if acquired later in life, bone marrow suppression, pneumonitis, encephalitis, encephalopathy, hepatitis, fever, skin rash, transplant rejection and death in bone marrow, kidney and liver transplant recipients on immunosuppression, disseminated infection, active CNS infection, pneumonitis, retinitis and contributes to death in AIDS; cultivated in mitogen-activated PBL or T cell lines; diagnosis: PCR of serum or plasma; treatment: foscarnet, ganciclovir

Human herpesvirus 7: ? causes some cases of roseola

Subfamily Gammaherpesvirinae

Lymphocryptovirus

Epstein-Barr virus: human herpesvirus 4; causes latent infection; circulating antibody prevents exogenous reinfection; forms circular episomes in nuclei of latently infected cells, transforms cells and causes heterophile mononucleosis; causes infectious mononucleosis (young adults), monocytic angina (older children, young adults, AIDS cases and organ transplant recipients), arthritis (in 5-10% of cases of infectious mononucleosis), encephalitis, adult hepatitis, hepatic granuloma, infusion

infection, non-pyogenic meningitis (Duncan's syndrome), Guillain-Barrè syndrome, maculopapular rash, exudative tonsillitis, nonpurulent conjunctivitis, ? urinary infection in infectious mononucleosis, hypersensitivity to mosquito bites; associated with Burkitt's lymphoma, nasopharyngeal carcinoma, B cell lymphomas, Hodgkin's disease, post-transplant lymphoproliferative disease, oral hairy leucoplakia; carried in blood associated with mononuclear cells; infects lymphocytes, causing mainly polyclonal B cell activation, triggering B lymphocytes to produce antibodies with a broad range of specificities, but also affecting T cells; persistence due to failure to display microbial antigen on infected cell surface; virally encoded complement receptor inhibits alternative complement pathway; down-regulation of cell surface adhesins (eg., LFA-3 and ICAM-1) prevents immune cell interactions; virally encoded cytokine (IL-10) homologue induces immunosuppression by inhibition of inflammatory cell formation; persists in lymphoid tissue (non-infectious, not shed to exterior, ? causing Burkitt's lymphoma) and salivary glands (infectious and shed to exterior); autoantibodies in infectious mononucleosis common (cytoskeletal antigen in 97%, nuclear antigen in 66%; also against cardiolipin, erythrocytes, lymphocytes, neutrophils, platelets, immunoglobulin, smooth muscle and thryoglobulin); increased infectiousness in abnormal host (clinical, subclinical, latent and persistent nonlatent infections); major host defence mechanisms basophil-mast cell (+), delayed type hypersensitivity activated macrophage (+++), direct cytotoxicity (+++); diagnosis: serology (indirect fluorescent antibody—Ig M and IgG $\geq$ 1:320—to virion capsid antigen, heterophil $\geq$ 1:56 (Paul-Bunnell test), ox cell absorption positive (Davidsohn's test), complement fixation test, ELISA, immunodiffusion) primary method, antigen detection not available, isolation not generally available

Rhabdinovirus

Human herpesvius &: Kaposi's sarcoma associated herpesvirus; probably causes tumours, including Kaposi's sarcoma, multicentric Castleman's disease and primary effusion lymphoma; transmitted by sexual contact, blood exchange, needle sharing

Family Mimiviridae

Mimivirus: diameter 600 nm; genome 1.2MB; exhibits binary multiplication; lacks capacity for complete protein translation; capsid

Family Papillomaviridae: *human papillomavirus,* many papilloma viruses of other mammals; circular double strand DNA, molecular weight 3-65X10^6 D (relatively small), 9 kb/strand in icosahedral, ether-resistant capsid 43-55 nm diameter, 72 capsomeres; penetrate host cell by endocytosis; replicate within nucleus of infected cell; produce latent and chronic infection in natural hosts; all tumourigenic; characteristically produce benign skin lesions in many species; cause progressive multifocal leucoencephalopathy (slow viral disease); do not have a conventional envelope, but viral antigens appear on surface of infected cells, which are then susceptible to immune lysis; oncogenic in experimental animals; persistent infection common; immunity cell-mediated immunity (++); diagnosis: hemagglutination inhibition, indirect fluorescent antibody (brain biopsy; antigen), complement fixation test (significant titre $\geq$ 1:8), tissue culture (primary human fetal glial cell culture), electron microscopy, histopathology

Human papillomavirus: 70 types in genera *Alphapapillomavirus, Betapapillomavirus, Mupapillomavirus, Nupapillomavirus* and in unclassified strains; causes or associated with genital warts (sexually transmitted; types 6, 11, 16, 18, 30, 31, 33-35, 39, 40, 42-45, 51-59), cutaneous (types 1-5, 7-10, 12, 14, 15, 17, 19-29, 36-38, 41, 46-50, 60), oral papillomas (types 13, 30, 32, 57), cervical malignancies (sexually transmitted; types 16, 18, 30, 31, 33, 35, 39, 45, 51, 52, 56), squamous cell carcinomas (including oral; types 5, 8, 16, 17, 20, 41, 48), melanoma (type 38), erythroplasia of Queyrat (type 16); clinical and persistent nonlatent infections in abnormal host; cultivated in organ culture of infected skin treated with TPA to increase keratinocyte differentiation; diagnosis: cytology; treatment: cryotherapy, electrosurgery, surgery, 5-fluorouracil, thiotepa, podophyllin, podofilox, imiquimod

Family Polyomaviridae

Polyomavirus: molecular weight 3.5X10^6 D, 5 kb/strand, 45 nm, 72 capsomeres, cyclic DNA; can produce cytopathic effects in tissue cultures; widely distributed among humans; progressive multifocal leucoencephalopathy is uncommon manifestation of a common polyoma virus infection of humans; persists in kidney tubules (infectious or noninfectious, shed to exterior); increased infectiousness in abnormal host; 6 genes; polyoma virus of mice, JC and BK viruses of humans, simian virus 40 of rhesus monkey (infection of nonpermissive cells results in permanent transfection of some cells only if viral DNA is integrated into host cell DNA), lymphotropic virus of African green monkey, viruses of mouse, rabbit, hamster and baboon

BK polyomavirus: human *Polyomavirus*; persists in kidney (non-infectious, shed to exterior), activated in pregnancy and immunosuppression; increased infectiousness in abnormal host (subclinical and persistent nonlatent, ? clinical and latent infections); ? cause of bladder carcinoma in transplant recipient

JC polyomavirus: causes progressive multifocal leucoencephalopathy; persists in kidney (non-infectious, shed to exterior), activated in pregnancy and immunosuppression; increased infectiousness in abnormal host (clinical and persistent nonlatent, ? subclinical and latent infections)

Simian virus 40: increased infectiousness in abnormal host; linked to non-Hodgkin's lymphoma

Family Poxviridae: large complex viruses; double strand DNA, molecular weight 160X10^6 D as internal nucleoid in brick-shaped (to ovoid) particle 200-260X250-390 nm with complex capsid symmetry and complex outer coat composed of 2

complete envelope membranes; replicate in cytoplasm of infected cells (host cell nucleus provides functional apparatus for maturation of envelope and internal components), producing eosinophilic inclusion bodies; antigenically complex; nucleoprotein shared by group; agglutination of chicken red cells by lipoprotein complex inhibited by immune serum; produce characteristic pox on chorioallantoic membrane of fertile eggs; protein and lipid present; relatively resistant to inactivation by chemicals (disinfectants) or by heat, cold or drying, inactivated by chloroform, variable inactivation by ether; common family and genus antigens; DNA-dependent RNA polymerase on virion; predilection for epithelial cells; antibodies provide some protection against certain strains; infection produces solid immunity; do not have a conventional envelope, but viral antigens appear on surface of infected cells, which are then susceptible to immune lysis; multiply in macrophages; control by elimination of viral transmission and immunisation; some species multiply on a variety of cultured cells

Subfamily Chordopoxvirinae: poxviruses of vertebrates

Capripoxvirus: 3 viruses of sheep and goats; causes goatpox (host range goats, humans; goats potential reservoir host)

Molluscipoxvirus

Molluscum contagiosum virus: causes chronic proliferative lesions (molluscum contagiosum, mouth lesions); clinical and persistent nonlatent infections in abnormal host; infection generally confined to epithelial surface of skin; host range humans, chimpanzees; humans potential reservoir host; diagnosis: cytology

Orthopoxvirus: virion 250X300 nm, brick-shaped, molecular weight 150-160X10^6 D, 231-242 kb/strand, AT/GC = 1.6

Cowpox virus: causes self-limited localised vesicular lesions; cattle source but host range includes humans and other mammals; occupational illness in livestock workers

Monkeypox virus: causes rare human infections which resemble smallpox (vesicular rash) but very limited spread; host range monkeys, humans, rodents; monkeys and rodents potential reservoir hosts; whitepox virus probably variant; diagnosis: electron microscopy

Vaccinia virus: artificially propagated virus used for human vaccination; host range humans, other mammals, birds, but no natural animal hosts; may have evolved from cowpox; causes abortion, encephalitis, nonpyogenic meningitis, skin lesions; increased infectiousness in abnormal host (clinical and persistent nonlatent infections); inhibits phagocytic (macrophage) oxidative burst, suppressor activity; escapes from phagosome; primary bodily defence mechanism cell-mediated immunity (+++); recovery from primary infection due to cell-mediated immunity; 160 genes

Variola virus: smallpox virus; double-stranded DNA, brick-shaped to ovoid, 250-390X200-260 nm; DNA-dependent RNA polymerase enzyme for early mRNA production; lipid solvent inactivated, resist inactivation by heat, cold, drying or disinfectants; cause alastrim (mortality 0.25%), smallpox (mortality 5-40%), abortion, hemorrhagic fever; infect epidermal cells; multiply in cell cytoplasm; short incubation period; result in death or complete recovery; if recovery, person usually immune; natural host man but monkeys and mice in host range, including as potential reservoir hosts; laboratory cultivation in animals (especially rabbit, calf, sheep), chick embryo, cell cultures (especially human embryonic kidney, monkey kidney, HeLa); diagnosis: complement fixation test, hemagglutination antibody technique, tissue culture of scrapings from skin lesions, vesicle fluid, pus, blood, crust

Poxviruses of Buffalo, Camel, Mouse, Elephant, Other Mammals: no human infections recognised

Parapoxvirus

Bovine papular stomatitis virus: causes bovine papular stomatitis; host range cattle, humans; potential reservoir host cattle

Orf virus: virion 160X260 nm; causes orf (contagious pustular dermatitis, contagious ecthyma) in sheep and other animal workers; host range sheep, goats, cattle, humans; potential reservoir hosts sheep, goats

Pseudocowpox virus: causes pseudocowpox (milker's nodes, milker's nodules; smooth or warty painless lesions and mild systemic complaints); source cattle; occupational illness in livestock workers

Yatapoxvirus

Yaba monkey tumor virus: causes Yaba monkey tumour pox; host range monkeys, humans; monkeys potential reservoir host

dsRNA Viruses

Family Reoviridae: RNA; double stranded; segmented; icosahedral capsid (60-80 nm)

Coltivirus: Colorado tick fever virus; tick-borne (*Dermacentor andersoni*); western US and Canada; causes 2 periods of abrupt onset high fever, chills, joint and muscle pains, severe headache, ocular pain, conjunctival injection, nausea, occasional vomiting in spring or summer, interrupted by brief, symptom-free interval; diagnosis: seroconversion, electron microscopy, immunofluorescence (antigen), PCR, IgM antibody-capture ELISA; treatment: symptomatic

Orbivirus: icosahedral, double capsid (outer skin-like), 70 nm diameter, double stranded RNA, 10 segments each molecular weight 0.3-2.7X10^6 D (total 12X10^6 D); 37 kb; infectivity stable with lipid solvents; 8 virion polypeptides; carried in blood associated with erythrocytes; includes Corriparta virus, Eubenangee virus, Kemeravo virus, blue tongue virus of sheep, African horse sickness virus

Orthoreovirus

Mammalian orthoreovirus: double stranded RNA; 70 nm, 72 capsomeres; icosahedral, double capsid, no envelope; 10-segmented; molecular weight 0.5-3X10^6 D/segment (total 15X10^6 D); 46 kb; infectivity stable with lipid solvents; 8 virion polypeptides; recombination by reassortment of subunits of genome; RNA polymerase must be introduced with virus for its replication; penetrates host cell by endocytosis; progeny virus stored in infected cell until its death, each transcribed into complementary, monocistronic messenger by virion transcriptase; inhibits phagocytic oxidative burst, escapes from phagosome; vector contaminated water polluted by animal or human feces (survival time weeks - months); causes acute respiratory illness, rhinitis, epidemic viral diarrhoea, neonatal hepatitis, maculopapular rash, nonpyogenic meningitis; produces mild illness in most infected persons; in mice, produces virus-induced diabetes as part of a polyendocrine disease with multiple organ reactive autoantibodies prevented by immunosuppression; diagnosis: tissue culture and inoculation of suckling mouse with material from feces and throat swab; other double stranded RNA viruses similar to *Orthoreovirus* include rice dwarf virus (molecular weight 15X10^6 D, 23 kb/strand, 10 segments) and cytoplasmic polyhedrosis of silkworms (molecular weight 15X10^6 D, 23 kb/strand, 10 segments)

Mammalian orthoreovirus 3: exanthem and pulmonary involvement

Rotavirus: 70 nm; icosahedral with double-shelled capsid, no envelope, double stranded RNA, probably 11 segments of molecular weight 0.23-2.04X10^6 D (total 10X10^6 D), 31 kb; infectivity stable with lipid solvents, fluorocarbon for 5 minutes at 37°C, pH $\geq$ 3 for 1 h at 37°C, 56°C for 1 h, –20°C for years; 10 virion polypeptides; survives 2-34 d in water (source animal and human feces); causes acute epidemic diarrhoea and/or vomiting (most common cause of infantile gastroenteritis; 41 M cases with 873,000 deaths (all < 5 y) globally annually; also traveller's diarrhoea; also in infant mice, calves, piglets, lambs, dogs, foals, infant rabbits, newborn deer, monkeys, goats, guinea pigs), upper respiratory tract infection, ? hakuri; replicates in intestinal epithelium; diarrhoea mechanisms not understood (? lactase deficiency $\rightarrow$ lactose intolerance); diagnosis: antigen detection primary method (ELISA (International Diagnostic Laboratories best commercial kit), latex agglutination), isolation (in differentiating human colon carcinoma cell line + trypsin) not generally available, seen by immune electron microscopy in stool, serology not practical for single cases

Unclassified dsRNA Viruses

Human picobirnavirus: ? causes epidemic viral diarrhoea

RETRO-TRANSCRIBING VIRUSES

Hepadnaviridae: double stranded DNA with RNA intermediate; cause infusion infections

Orthohepadnavirus

Hepatitis B virus: small icosahedral particles (nucleic acid-free, possibly aggregate of virus capsomeres) about 22 nm diameter (Australia antigen) in acute phase serum hepatitis; virus particle (including nucleic acid) possibly about 2 nm diameter; 22 nm sphere buoyant density (CsCl) 1.2 g/cm^3, sedimentation coefficient 543, protein, glycoprotein, lipid; filamentous forms buoyant density (CsCl) 1.2 g/cm^3; Dane particles (42 nm spheres) buoyant density (CsCl) 1.25 g/cm^3, sedimentation coefficient 58-59, protein, glycoprotein, lipid, circular interrupted double strand DNA; core particles buoyant density (CsCl) 1.36 g/cm^3, sedimentation coefficient 1105, protein, circular interrupted double strand DNA; contains both single strand and double strand DNA; envelope from infected cell; not readily grown in vitro; causes serum hepatitis (long incubation hepatitis), cirrhosis, abortion, arthritis, Guillain-Barré syndrome, hemorrhagic fever, hepatic granuloma, infusion infections, myocarditis and pericarditis, non-pyogenic meningitis, rhabdomyolitis, stillbirth; associated with hepatocellular carcinoma; usually transmitted in blood and in pooled plasma products (inactivated by severe terminal heat or solvent-detergent treatment; sporadic transmissions after pasteurisation) by parenteral inoculation, but also sexually; incubation period 60-160 d; onset insidious; fever > 38°C uncommon; year-round; all ages, commonest in adults; virus not demonstrated in feces; primary bodily defence mechanism humoral immune responses (antibody ++), cell-mediated immunity (+); antigen-antibody complexes circulate in serum, deposit in tissue, bind complement and produce injury (glomerulonephritis, arthritis, vasculitis) in a classic model of viral immune complex disease in humans; acute arthritis due entirely to host immune response; necrotising vasculitis with chronic infection (important that virus persists systemically, host immune response; ? cross reactive antigen not important; sequence: virus replication systemically, immune response, immune complexes, kidney and vascular deposits of circulating immune complexes, inflammation, virus persistence); viral surface antigens in extracellular fluids combine with and 'divert' antibodies; persists in liver (virus shed into blood, which remains infectious); serum autoantibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced; increased infectiousness in abnormal host (clinical, subclinical and persistent nonlatent infections); decreases polymorphonuclear bactericidal, chemotactic and oxidative functions; diagnosis: reverse passive indirect hemagglutination, radioimmunoassay (antibody and antigen), ELISA (antibody and antigen), counterimmunoelectrophoresis; HBsAg (surface antigen) appears 30-50 d after infection; detection of HBsAg in blood, less often in feces, urine, semen, bile; detection of HBsAg 60 d - years; HBsAg contains strain specific antigenic determinants that may vary geographically and are combinations of several determinants (multiple serologic types of coat proteins); prophylactic value of γ-globulin good if titre of anti-HBs antigen high (passive immunity)

Family Retroviridae: about 100 nm diameter, molecular weight 6-7X10^6 D; surface membrane site of nucleocapsid development; diploid viruses; genome alternates between RNA in virion and proviral DNA in host cell; 2 identical messenger single strand RNA segments (positive strand), each transcribed into DNA by reverse transcriptase in virion; functional mRNAs transcribed from this; ? cause mucocutaneous lymph node syndrome, implicated in schizophrenia

Subfamily Orthoretrovirinae

Alpharetrovirus

Avian leukosis virus: causes lymphoid, hematopoietic, and vascular neoplasms

Avian sarcoma virus: causes renal, hepatic and connective tissue neoplasm

Rous sarcoma virus: molecular weight 3.5X10^6 D, 10.5 kb/strand, 1 segment, positive polarity

Deltaretrovirus

Human T-lymphotropic virus 1: causes adult T cell leukemia, infusion infections, HTLV-I-associated myelopathy, T cell lymphoma, tropical spastic paraparesis, ? multiple sclerosis; affects mainly T helper cells; endemic in SE USA, Japan, S America, Carribean; transmitted in blood and sexually; diagnosis: competitive ELISA, radioimmunoassay, immunoprecipitation

Human T-cell leukemia virus 2: causes T cell hairy cell leukemia, infusion infections; endemic in England and New York City in i.v. drug abusers, sexually transmitted

Gammaretrovirus

Murine leukemia-related retroviruses: carried in blood associated with platelets; kidney deposits of circulating immune complexes may cause glomerulonephritis

Feline leukemia virus: infects cats; kidney deposits (may cause glomerulonephritis) and vascular deposits of circulating immune complexes; diagnosis: isolation, immunofluorescent antibody, ELISA

Lentivirus

Equine Lentivirus Group

Equine infectious anaemia virus: infects horses; infects macrophages; autoimmune reactions against retroviral antigens on the surface of erythrocytes cause hemolytic anemia; kidney deposits (causing glomerulonephritis) and vascular deposits of circulating immune complexes; diagnosis: agar gel immunodiffusion test

Ovine/caprine Lentivrus Group

Caprine arthritis encephalitis virus: causes retrovirus-mediated synovitis in goats that resembles rheumatoid arthritis; multisystem disease may be associated

Visna/Maedi virus: 'slow virus'; infects sheep, causing maedi and visna, progressive pneumonia; infects lymphocytes and macrophages

Primate Lentivirus Group

***Human immunodeficiency virus* (HIV):** 110 nm; ssRNA; envelope; causes acquired immunodeficiency syndrome (AIDS), AIDS dementia complex (HIV encephalopathy), AIDS enteropathy, Guillain-Barrè syndrome, reactive arthritis, vasculitis, teratogenic effects; produces profound helper T cell dysfunction; macrophages also affected; decreases polymorphonuclear chemotactic and secretory functions; serum antibodies against DNA, erythrocytes, lymphocytes, neutrophils, platelets and immunoglobulins produced (may reflect coinfections with other viruses and microorganisms as well as an effect of HIV; in some cases, antibody-related autoimmune diseases may appear); transmitted in blood and in pooled plasma products (inactivated by severe terminal heat and solvent-detergent treatment) and sexually; cultivated in mitogen-activated PBL or T cell lines; diagnosis: ELISA, Western blot, p24 antigen capture, culture of peripheral blood lymphocytes, test for proviral DNA; treatment: zidovudine, didanosine, zalcitabine, ganciclovir

Human immunodeficiency virus 1: causes AIDS and AIDS-related complex; endemic in Central Africa, Europe, USA

Human immunodeficiency virus 2: causes AIDS; endemic in W Africa, Cape Verde

Simian immunodeficiency virus: causes AIDS-like syndromes in Asian monkeys, affecting T, B and NK cells; African monkeys natural hosts, disease not produced

Subfamily Spumoretrovirinae

Spumavirus: foamy virus group; > 4 syncytial and foamy viruses of humans, monkeys, cattle and cats; includes avian reticuloendotheliosis virus (chicken syncytial virus); no disease known in humans

ssDNA Viruses

Family Parvoviridae: single strand DNA, molecular weight 1.4-2.2X10^6 D in icosahaedral, ether-resistant capsids about 18-26 nm, 32 capsomeres; positive and negative polarity

Subfamily Parvovirinae

Dependovirus: adeno-associated virus; defective, cannot replicate in absence of helper adenovirus; human (types 1-3), monkey (type 4), > 4 others of cattle, dogs, birds; molecular weight 1.5X10^6 D, 4.5 kb/strand, 20 nm, 12 capsomeres, single strand DNA; useful for gene therapy; integrates into chromosome

Erythrovirus

Human parvovirus B19: 24 nm; ssDNA; no envelope; transmission by droplets and by pooled plasma products (solvent-detergent treatment ineffective, effectiveness of heat unknown) and congenital; causes aplastic crisis, erythema infectiosum

('fifth disease', 'slapped face'), stillbirth (rare), anemia, arthritis (? including rheumatoid arthritis), hydrops foetalis, polymorphous rash, pneumonia, hepatitis, myocarditis; cultivated in dividing erythrocyte progenitors or megakaryocytic cell line + erythropoitin and GM-CSF; diagnosis: PCR, dot hybridisation, capture ELISA on serum

Parvovirus: survival time in water unknown (source human feces); causes epidemic viral diarrhoea (in 47% of infections), gastroenteritis

***Parvovirus*-like agents:** cause water-borne gastroenteritis (19% of outbreaks)

SSRNA VIRUSES

SSRNA NEGATIVE-STRAND VIRUSES

Arenaviridae: molecular weight $3.5X10^6$ D; contained in a set of granules about 20 nm diameter similar to ribosomes; particle 50-300 nm diameter (average 110-130 nm) with lipid envelope with surface spikes; develop in cytoplasm of infected cells; surface membrane site of helical nucleocapsid development; single strand RNA; spherical, pleomorphic, 2 segments virus specific 3.6 and $1.6X10^6$ D (11 and 4.8 kb); in 3 species, host RNA also in virions; 2 glycoproteins 72,000 and 1200 D; lipid solvents inactivate; unstable; no hemagglutination; best animal hosts various rodents; budded from surfaces of cells; geographically restricted to range of host mammals; able to code for new antigens on surface of infected cells; person-to-person transmission rare

Arenavirus: single strand RNA; envelope from infected cell; diameter of virion 50-300 nm; normally infects rodents; may give serious disease in man

New World Arenaviruses

***Guanarito virus*:** causes Venezuelan hemorrhagic fever; Venezuela

***Junin virus*:** causes Argentinian hemorrhagic fever; Argentina; case-fatality rate 20%; no arthropod vector; rodent transmission; diagnosis: serology; treatment: postconvalescent plasma

***Machupo virus*:** causes Bolivian hemorrhagic fever; Bolivia; case-fatality rate 20%; rodent transmission; diagnosis: serology

***Tacaribe virus*:** headache, fever, neuralgia, hemorrhagic signs; S and Central America

***Lassa virus*:** causes Lassa fever (hemorrhagic fever), abortion, encephalitis, myocarditis and pericarditis, adult hepatitis; found in W and Central Africa; maintained in nature by rodent, transmitted by rodent, easily transmitted from person to person; diagnosis: isolation from blood, throat or urine, serology (fluorescent antibody staining of conjunctival scrapings); treatment and prophylaxis: ribavirin

***Lymphocytic choriomeningitis virus*:** normally infects mice; may give serious disease in man; causes 'influenza-like illness', birth defects, encephalitis, non-pyogenic meningitis, parotitis and submandibular sialadenitis; multiplies in macrophages; carried in blood in platelets, leucocytes and plasma; infects lymphocytes and macrophages (affects accessory function of macrophages); antibody of poor specificity or affinity fails to neutralise or opsonise; viral invasion of lymphoid tissue leads to suppressor T cell induction or clonal deletion of T cells; persistent, but harmless, carriage of virus for laboratory rodents; persistent infection leads to a continuous immune complex formation and trapping, causing glomerulonephritis, vasculitis, and uveitis, as well as possibly deleterious production of autoantibodies and interferon; recovery from primary infection due to cell-mediated immunity (antibody-initiated, complement-dependent lysis requiring specific antiviral IgG and alternative pathway of complement)

Family Bunyaviridae: 90-100 nm diameter, molecular weight $6\text{-}7X10^6$ D; arboviruses; spherical, enveloped, helical nucleocapsid; single stranded RNA, 3 segments of 4, 2 and $0.8X10^6$ D (12, 6 and 2.4 kb); 2 glycoproteins 115,000 and 38,000 D, 1 nonglyoxylated protein 19,000 D; lipid solvents inactivate; unstable below pH 7; hemagglutinate 1 d chick or goose red blood cells; cause encephalitis; best animal host suckling mice, chicken

Hantavirus: Asia, Balkans, former Soviet Union, Europe, USA, Africa; rodents, bats, birds reservoir; transmission via aerosol; many members; diagnosis: immunofluorescent antibody test, ELISA; treatment: ribavirin; prevention: combined Hantaan/Puumula vaccine

Andes virus: causes Hantavirus pulmonary syndrome

Bayou virus: causes Hantavirus pulmonary syndrome

Black Creek Canal virus: causes Hantavirus pulmonary syndrome

Hantaan virus: causes hemorrhagic fever with renal syndrome (epidemic hemorrhagic fever)

New York virus: cause Hantavirus pulmonary syndrome

***Puumala virus*:** causes nephropathia epidemica (mild form of hemorrhagic fever with renal syndrome occurring in Scandinavia); diagnosis: serology, histology; treatment: ribavirin

Seoul virus: causes Korean hemorrhagic fever

Sin nombre virus: causes Hantavirus pulmonary syndrome

Nairovirus

Crimean-Congo haemorrhagic fever virus: causes Crimean-Congo hemorrhagic fever (headache, fever, myalgia, hemorrhagic signs, meningoencephalitis, nonpurulent conjunctivitis); Africa, Asia, Southern former Soviet Union; mosquito-borne; diagnosis: isolation of virus from blood, 4X rise in antibody titre, presence and decline of IgM antibody

Orthobunyavirus

Bunyamwera: mosquito vector; headache, fever, myalgia, fever only or no symptoms; Uganda, S Africa, India, Malaya, Colombia, Brazil, Trinidad, W Africa, Finland, USA

California Encephalitis Virus: causes California encephalitis (≈ 60 cases (< 1 death)/y; *Aedes melaninon* vector; ground squirrel principal vertebrate host; California, Texas, Utah)

Bunyavirus La Crosse: causes La Crosse encephalitis; mosquito (*Aedes triseriatus*) vector; chipmunk and squirrels principal vertebrate hosts; Upper Mississippi River Valley

Tahyna virus: *Culiseta annulata* and *Aedes* vectors; hares principal vertebrate host; Europe

Phlebovirus: sandfly fever virus and other viruses of humans and animals, including of sheep and other ruminants, which may cause human disease (Phlebotomus fever, nonpurulent conjunctivitis)

Rift Valley fever virus: causes Rift Valley fever (headache, fever, myalgia, joint pains, hemorrhagic signs, rash, 'influenza-like illness', encephalitis in <1% of infections); mosquito-borne; Subsaharan Africa, Middle East, India, Egypt, Sudan; diagnosis: serology, isolation by tissue culture or inoculation of suckling mice during febrile stage

Uukuniemi virus: infects rodents and ticks; Finland

Order Mononegavirales

Family Bornaviridae

Bornavirus: Borna disease virus; causes progressive polioencephalomyelitis in horses and sheep; possibly linked to schizophrenia-like disease and major depressive disorder in humans

Family Filoviridae

Ebola virus: causes Ebola hemorrhagic fever; Subsaharan Africa; means of transmission unknown; diagnosis: antigen test by immunofluorescent agglutination test, antibody ELISA, reverse transcriptase polymerase chain reaction

Marburgvirus: causes Marburg hemorrhagic fever; Subsaharan Africa; means of transmission unknown; acquired after exposure to tissues of infected African monkeys; diagnosis: direct visualisation on electron microscopy of infected tissues, virus specific immunofluorescence or electron microscopy of isolate (grows readily in Vero cells) from blood or serum or suspensions of heart, kidney, liver or spleen, complement fixation test

Family Paramyxoviridae: single negative strand RNA antimessenger on which virion transcriptase initiates transcription at single promoter to yield 5-8 complementary messengers (positive strand); molecular weight 5-7X10^6 D (17-20 kb) in an internal coiled ribonucleoprotein helix 18 nm diameter (except *respiratory syncytial virus*—14 nm) embedded in lipid of host cell origin, which also contains viral hemagglutinin; particle about 125-300 nm (range 100-800 nm) diameter with surface spikes; RNA synthesised in nucleus of infected cell, other components in cytoplasm; virus maturation at cell surface; ether sensitive; hemagglutinate red cells; penetrate host cells by fusion; do not require intact nucleus to reproduce; nucleocapsid localised in cytoplasm, not fragmented; virion (viral-coded) RNA polymerase; no separate hemagglutinin and neuraminidase; hemagglutinins attach to host cell nuclear membrane before budding of virus during viral replication; neuraminidases induce antibody that decreases size, but not number, of plaques in vitro; filamentous forms observed; hemolysin present (except in *respiratory syncytial virus*); prominent cytoplasmic inclusions (also nuclear in *measles virus*); syncytial formation; disrupt with lipid solvents; cytoplasm site of multiplication

Subfamily Paramyxovirinae

Avulavirus

Newcastle disease virus: molecular weight 6X10^6; 18 kb/strand; 1 segment negative polarity 18 nm diameter, virion 125-250 nm; causes disease in fowl, non-purulent conjunctivitis in man; inhibits phagocytic oxidative burst

Henipavirus

Hendra virus: equine morbillivirus; causes respiratory disease in horses and humans

Nipah virus: causes encephalitis (often fatal); spread from pigs to humans; Malaysia and Singapore; diagnosis: immunohistochemistry + serology

Morbillivirus

Canine distemper virus: causes distemper in dogs; multiplies in macrophages, causing profound suppression of T and B cells and macrophages

Measles virus: more contagious than mumps; hemagglutination +, hemadsorption +, hemolysis +, neuraminidase –; 1 antigenic type; causes measles (morbilli, rubeola), anterior uveitis, bronchopneumonia, coryza, catarrh, croup, 6-7% of encephalitis, epidemic viral diarrhoea, neonatal hepatitis (fatal in children with leukemia), 4% of non-pyogenic meningitis, mouth lesions, myocarditis and pericarditis, otitis media, giant cell pneumonia with exanthem, pneumonitis, mesenteric lymphadenitis (in 15% of hospitalised cases), subacute sclerosing panencephalitis (chronic neurologic condition with characteristics of both 'chronic' and 'slow' infection), maculopapular rash, roseola-like illness, urinary infection, nonpurulent conjunctivitis; atypical measles follows infection in persons previously immunised with formalin-inactivated measles vaccine (gives polymorphous rash); clinical and persistent nonlatent infection in abnormal host (T helper lymphocyte dysfunction); enters across epithelial surfaces of respiratory tract and conjunctiva and subsequently spreads through body; multiplies in macrophages; infects lymphocytes, affecting functions (not 'luxury' functions) of T, B and NK cells; decreases

polymophonuclear chemotactic functions; carried in blood associated with mononuclear cells; loss of viral antigen by capping; recovery from primary infection due to cell-mediated immunity, resistance to reinfection due to antibody; persists in brain (may be infectious, not shed to exterior), causing subacute sclerosing panencephalitis; > 66% of cases have antibodies to smooth muscle and cytoplasmic filaments; serum autoantibodies against DNA, lymphocytes, insulin, pancreatic β-cells and heart muscle (in acute myocarditis only) also produced; diagnosis: hemagglutination inhibition (significant titre ≥ 1:10 or 4X rise), complement fixation test, staphylococcal protein A adsorption (specific IgM), sucrose gradient ultracentrifugation, ELISA (IgG, IgM), tissue culture (WI38, primary monkey kidney, Hep2; no growth in human diploid fibroblasts; vacuolated, syncytial giant cells; rarely isolated but may be cultured from throat swab or washings collected soon after rash appears; verified by neutralisation test, fluorescent antibody); treatment: ribavirin

Peste-des-petite-ruminants virus: causes disease in sheep and goats

Rinderpest virus: causes rinderpest in cattle

Respirovirus

Human parainfluenza 1: nearly all cases in children < 5 y; epidemic usually every other year; causes bronchitis, acute bronchiolitis and bronchopneumonia, pneumonia (++++), croup (++++), minor URTI (++), acute laryngitis, common or feverish cold (++), 'influenza-like illness' (+++), tracheobronchitis, febrile nasopharyngitis, parotitis and submandibular sialadenitis; 3% of respiratory viral isolates in hospitalised children; also epidemic viral diarrhoea (in 15% of cases), otitis media, rhabdomyolysis, roseola-like illness; hemagglutination +, hemadsorption +, hemolysis +, neuraminidase +, antigenic relationship to mumps; decreases polymorphonuclear bactericidal and secretory functions; diagnosis: isolation primary method (primary monkey kidney +++, Hep2 +, human diploid fibroblasts negative; 6-11 d to isolation, no cytopathic effect; hemadsorption at 4°C < at 20°C), antigen detection described but not generally available, paired sera required for serology (hemagglutination inhibition, fluorescent antibody, complement fixation test, radioimmunoassay, ELISA); treatment: ribavirin aerosol (when warranted)

Human parainfluenza 3: about ½ of cases in children < 1 y; endemic; causes minor URTI (++), acute laryngitis, bronchitis, acute bronchiolitis and bronchopneumonia, pneumonia (++++), croup (+), common or feverish cold (++), tracheobronchitis, acute sinusitis, parotitis and submandibular sialadenitis, influenza-like illness (+), meningitis; 12% of respiratory viral isolates in hospitalised children; hemagglutination +, hemadsorption +, hemolysis +, neuraminidase +, antigenic relationship to mumps; decreases polymorphonuclear bactericidal and secretory functions; diagnosis: isolation primary method (primary monkey kidney +++, Hep2 +, human diploid fibroblasts negative; 6-11 d to isolation, no cytopathic effect or focal rounding and multinucleate giant cells (types 2 and 3); hemadsorption at 4°C < at 20°C), antigen detection described but not generally available, paired sera required for serology (hemagglutination inhibition, fluorescent antibody, complement fixation test, radioimmunoassay, ELISA); treatment: ribavirin aerosol (when warranted)

Rubulavirus

Human parainfluenza 2 virus: about ½ of cases in children < 5 y; epidemic usually every other year; causes croup (+), tracheobronchitis, febrile nasopharyngitis, acute sinusitis, acute chest infection; 0.9% of respiratory viral isolates in hospitalised children; diagnosis: isolation primary method (primary monkey kidney +++, Hep2 +, human diploid fibroblasts negative; 6-11 d to isolation, focal rounding and multinucleate giant cells; hemadsorption at 4°C < at 20°C), antigen detection described but not generally available, paired sera required for serology (hemagglutination inhibition, fluorescent antibody, complement fixation test, radioimmunoassay, ELISA); treatment: ribavirin aerosol (when warranted)

Human parainfluenza virus 4: about ½ of cases in children < 5 y; endemic; causes common cold, minor URTI, pertussis-like syndrome, meningoencephalitis; 0.6% of respiratory viral isolates in hospitalised children

Mumps virus: hemagglutinins and neuraminidases found on a single glycoprotein antigen; hemagglutination +, hemadsorption +, hemolysis +, neuraminidase +; 1 antigenic type, antigenic relationship to *human parainfluenza 1*; causes mumps, anterior uveitis, arthritis, 6-10% of encephalitis, hydrocephalus and mental retardation, 1-4% of non-pyogenic meningitis, meningoencephalitis, myocarditis and pericarditis (in 0.04% of mumps cases), oophoritis, orchitis, pancreatitis, epidemic parotitis, respiratory infections; > 66% of cases have antibodies to smooth muscle and cytoplasmic filaments; serum autoantibodies against DNA, lymphocytes, insulin, pancreatic β-cells and heart muscle (in acute myocarditis only) also produced; immunisation with live attenuated virus against mumps may be successfully combined with immunisation against measles and rubella; rarely isolated but can be cultured from blood, saliva, throat swab, secretions from Hansen's duct, CSF, urine; grows in primary monkey kidney (+++), human diploid fibroblasts (+), not in Hep2; 7 d to isolation, enlarged syncytial giant cells; diagnosis: complement fixation test, indirect fluorescent antibody titre for IgG and IgM, ELISA (IgM), hemadsorption, passive hemagglutination, hemagglutination inhibition, neutralisation test (not routine)

Subfamily Pneumovirinae

Metapneumovirus

Human metapneumovirus: causes mild to severe respiratory disease in children (bronchiolitis in 68%, pneumonitis in 17%)

Pneumovirus

Human respiratory syncytial virus: hemagglutination +, hemadsorption –, hemolysis –, neuraminidase – 1 antigenic type; causes acute respiratory illness—acute bronchiolitis, bronchopneumonia, pneumonia and pneumonitis in infants (+++), common or feverish cold (++), URTI (++), croup (+), influenza-like illness (+), bronchitis, rhinitis, acute exudative tonsillitis; causes airway hyperresponsiveness and enhanced airway sensitisation to allergen; 66% of respiratory viral isolates in hospitalised children; major cause of lower respiratory tract infection in young children; most frequent nosocomial infection on pediatric wards; decreases polymorphonuclear bactericidal, chemotactic, oxidative and secretory functions; natural immunity incomplete; diagnosis: isolation primary method (primary monkey kidney +++, human diploid fibroblast +, Hep2 +++, 6-8 d for isolation, enlarged, glassy, syncytial giant cells or granular rounded cells; verified by fluorescent antigen, neutralisation test, ELISA), antigen detection useful for rapid diagnosis (ELISA (Vidas sensitivity 66%, specificity 94%), radioimmunoassay), paired sera required for serology; treatment: ribavirin

Family Rhabdoviridae: negative polarity single strand RNA (noninfectious), molecular weight 3-4.6X10^6 D (11-24 kb) in an internal coiled ribonucleoprotein helix 18-50 nm embedded in lipid of host cell origin, making a bullet-shaped particle 60-80X130-240 nm with surface spikes; penetrate cells by endocytosis; most harmless to humans; virion enzyme (RNA dependent) RNA transcriptase; lipid solvents disrupt virions, inactivate infectivity; maturation by budding at cytoplasmic membranes; hosts wide range of mammals, fish, invertebrates and plants; no common antigens; diagnosis: antigen detection and isolation in reference laboratories primary methods, serology useful for assessment of immunity

Dimarhabdovirus Supergroup

Vesiculovirus: several vesicular stomatitis viruses infecting horses, cattle, swine and occasionally humans; molecular weight 4X10^6 D, 13 kb/strand, 1 segment, negative polarity, virion 68X175 nm, bullet-shaped

Lyssavirus

Rabies virus: causes rabies, encephalitis, myocarditis and pericarditis; transmitted by bite from infected animal; persistent infection of glands, etc inaccessible to circulating antibody

Family Orthomyxoviridae: single stranded RNA in several distinct non-overlapping messenger (negative strand) pieces, each 1 gene, each separately transcribed by virion transcriptase into complementary, noncistronic messenger; molecular weight 2-5X10^6 D in 6 separable components, in an internal coiled ribonucleoprotein helix 6-15 nm diameter embedded in lipid of host cell origin, which also contains viral components, hemagglutinin and neuraminidase; protein component of greatest molecular weight (73%); particle about 80-120 nm diameter with surface spikes; ribonucleoprotein synthesised in nucleus of infected cell, other components in cytoplasm; matures at cell surface; ether sensitive; hemagglutinate red cells (human group O, chick, guinea pig); grow in chick embryo amniotic cavity and in cultures of monkey kidney cells; ribonucleoprotein is complement fixing antigen common to all strains within A, B, C types; complex antigenic makeup of major and minor antigens and rapid antigenic variation allow virus to recirculate throughout community (antigenic drift by small mutational changes, antigenic shift by hybridisation between human virus and virus from animal reservoirs); penetrate cell by endocytosis; nucleoprotein localised in nucleus; virion (viral-coded) RNA polymerase; separate hemagglutinin and neuraminidase (enzyme that cleaves N-acetylmuramic acid, glycoprotein coded by discrete segment of RNA, thought to enhance penetration of mucus, capable of varying independently of viral hemagglutinin); filamentous forms common; hemolysin absent; prominent cytoplasmic inclusions absent; syncytial formation; regularly produce pandemics; diagnosis: isolation primary method, antigen detection described but not generally available, paired sera required for serology

Influenzavirus A: H_0N_1 (A_0, human), H_1N_1 (A_1), H_2N_2 (A_2), H_3N_2 (A_{HK}, A_3), $H_{sw}N_1$ (swine), $H_{eq}N$ (2 equine), $H_{av}N$ (8 avian); causes influenza (++++), croup (+++), pneumonia (++), URTI (++), common or feverish cold (+), bronchitis, acute bronchiolitis and bronchopneumonia, laryngotracheitis, pneumonitis, coryza, tracheobronchitis, acute sinusitis, acute exudative tonsillitis, otitis media, parotitis and submandibular sialadenitis, 6% of nonpyogenic meningitis, postinfectious encephalomyelitis, Guillain-Barré syndrome, myocarditis and pericarditis, nonpurulent conjunctivitis, Reye's syndrome; 4% of respiratory viral isolates in hospitalised children; clinical infection in abnormal host; inhibits lysosome-phagosome fusion and phagocyte oxidative response; pandemics in 1890-1892 (H_2N_2), 1902-1903 (H_3N_2), 1918-1919 ($H_{sw}N_{sw}$, swine-like; 22 M deaths), 1929 (H_0N_1), 1947 (H_1N_1, A prime), 1957-1958 (H_2N_2, Asian, A/Japan/57; 70,000 excess deaths), 1968-69 (H_3N_2, Hong Kong, A/Hong Kong/68; 34,000 excess deaths), 1973 (A/England/72; 25,000 excess deaths), 1976 (A/Victoria/75; 27,000 excess deaths), 1977 (H_1N_1, Russian); detection: hemagglutination inhibition, indirect fluorescent antibody titre, radioimmunoassay, ELISA, tissue culture (WI38, primary monkey kidney); treatment: ribavirin aerosol (i.v. in myocarditis and pericarditis), amantadine, rimantidine

Influenzavirus B: causes influenza, bronchitis, acute bronchiolitis and bronchopneumonia, tracheobronchitis, common or feverish cold, coryza, croup, pneumonia, pneumonitis, URTI, nonexudative pharyngitis and tonsillitis, acute laryngitis, otitis media, myocarditis and pericarditis, hepatic granuloma, nonpurulent conjunctivitis; 2% of respiratory viral isolates in hospitalised children; diagnosis: radioimmunoassay, ELISA; treatment: ribavirin aerosol (i.v. in myocarditis and pericarditis)

Influenzavirus C: causes influenza, upper respiratory tract infection, coryza, pneumonia

ssRNA Positive-StrandViruses, No DNA Stage

Family Astroviridae: RNA; naked icosahedral nucleocapsid; single stranded; positive polarity

Mamastrovirus

Human astrovirus: causes gastroenteritis

Family Caliciviridae: diameter of virion 35-39 nm, molecular weight of nucleic acid in virion 2.6-2.8X10^6 D; cause gastroenteritis

Norovirus: 27 nm; round; density 1.38-1.41 g/cm^2; stable to 20% ether for 24 h, pH 2.7 for 3 h, 60°C for 30 minutes; causes acute epidemic diarrhoea and/or vomiting; ? replicates in intestinal epithelium; Norwalk virus (USA), Hawaii virus (USA), Ditchling virus (England), Cochle virus (England), Montgomery County virus (USA), W virus (England), Parramatta virus (Australia), Colorado virus (USA), small round virus (Japan), Marin County virus (USA); 40% of outbreaks in hospitals and 39% in residential care facilities; 85% of transmission person-to-person

Sapovirus: causes gastroenteritis

Sapporo virus: causes epidemic viral diarrhoea

Flaviviridae: RNA; enveloped; icosahedral nucleocapsid; single stranded; positive polarity

Flavivirus: 25-50 nm diameter in a lipid envelope; single stranded RNA; molecular weight 3X10^6 D; replicates in cytoplasm and matures by budding from intracytoplasmic membranes; arboviruses group B; 26 mosquito-borne members, including Alfuy virus, dengue, Edge Hill virus, Japanese B encephalitis, Kokobera virus, Koutango virus, Kunjin virus, Murray Valley encephalitis, St Louis encephalitis, Stratford virus, Usutu virus, West Nile fever, yellow fever; 11 tick-borne viruses, including Kyasanur Forest disease, Omsk hemorrhagic fever, European and Far Eastern tick-borne encephalitis; and 17 vector-unassociated viruses

Subgenus *Dengue Virus Group*

Dengue virus species 1-4: cause dengue fever (headache, fever, myalgia, maculopapular rash in 31% of cases), dengue hemorrhagic fever (hemorrhagic rash), dengue shock syndrome (prostration), nonpurulent conjunctivitis; antibody bound to microbe enhances infection of phagocyte; affects macrophage suppressor activity; vectors *Aedes aegyptii, Aedes scutellaris, Aedes katherinensis* and *Aedes albopictus* mosquitoes; host humans; widespread (S and SE Asia, Pacific Islands, Central and S America, N Australia, New Guinea, Greece, Caribbean Islands, Nigeria); diagnosis: culture (sensitivity 30-80%), ELISA (IgM positive in 80% by fifth day), immunochromatographic card assay (sensitivity 99% in primary cases, 94% in secondary, specificity 93%), reverse transcription-polymerase chain reaction (being evaluated), hybridisation assay (being evaluated); controlled by mosquito control; live vaccine under test

Subgenus *Japanese Encephalitis Virus Group*

Japanese encephalitis virus: mosquito (*Culex triteniorhynchus* in Asia, *Culex annulirostrus* in Australia) vector and reservoir; other reservoirs pigs, water birds; causes encephalitis (> 50,000 cases annually; fatality rate > 25%); Japan, Guam, E Asian mainland, Malaya, India, Pakistan, Australia; epizootic in temperate and subtropical areas, enzootic in tropical

Koutango virus: Japanese encephalitis serological complex; Africa

Kunjin virus: Japanese encephalitis serological complex; vectors and reservoirs as for ***Murray Valley encephalitis virus***; causes Australian encephalitis; Australia, Papua New Guinea, Borneo

Alfuy virus: Japanese encephalitis serological complex; Australia

Murray Valley encephalitis virus: Japanese encephalitis serological complex; mosquito (*Culex annulirostrus*) vector; water birds reservoir; causes Australian encephalitis; Australia, Papua New Guinea, eastern Indonesia

St Louis encephalitis virus: Japanese encephalitis serological complex; vector *Culex* mosquito; host birds, especially English sparrows; Western Hemisphere (USA, Trinidad, Panama); causes St Louis encephalitis (≈ 60 cases (4 deaths)/y; more severe in older people); diagnosis: IgM and IgG indirect immunofluorescent serum antibody; controlled by mosquito control

Usutu virus: Japanese encephalitis serological complex; Africa

West Nile virus: Japanese encephalitis serological complex; mosquito vector; birds amplifying host; causes headache, fever (may be hemorrhagic), myalgia, rash, lymphadenopathy, meningoencepahlitis; Egypt, Israel, India, Uganda, S Africa, Southern Europe, Western and South-Western Asia, USA, Australia

Subgenus *Kokobera Virus Group*

Kokobera virus: Japanese encephalitis serological complex; Australia, Papua New guinea

Stratford virus: Japanese encephalitis serological complex; Australia

Subgenus *Mosquito-borne Viruses*

Ilheus virus: mosquito vector; causes encephalitis; Brazil, Guatemala, Trinidad, Honduras

Subgenus *Rio Bravo Virus Group*

Rio Bravo virus: found in bat salivary gland; unrecognised vector; causes encephalitis; California, Texas

Subgenus *Tick-borne Encephalitis Virus Group*

Kyasanur Forest disease virus: causes Kyasanur Forest disease (hemorrhagic fever); India; tick transmission

Louping ill virus: causes louping ill in Great Britain

Omsk haemorrhagic fever virus: causes Omsk hemorrhagic fever; Central Russia, Romania; tick transmission

Powassan virus: vectors *Ixodes cookei, Ixodes marxi, Ixodes persulcatus, Ixodes ricinus, Ixodes spinipalpus, Dermacentor andersoni;* host rodents (primarily woodchucks in USA), birds, goats, cattle; NE and Central Europe, Canada, Northern USA; causes encephalitis (case-fatality rate 10-20%); prevented by protection from tick bite; controlled by tick control

Subgenus *Yellow Fever Virus Group*

Edge Hill virus: related to yellow fever virus; Australia

Yellow fever virus: causes yellow fever (hemorrhagic fever, prostration, hepatitis, nephritis); carried in blood free in plasma; recovery from primary infection due to antibody; vector mosquito (*Aedes aegyptii* and other *Aedes*); host humans and nonhuman primates; tropical America, sub-Saharan African, Trinidad; diagnosis: serology (antigen in blood by ELISA, specific IgM or rise in titre by complement fixation test, hemagglutination inhibition antibody technique, neutralisation antibody titre), isolation in tissue culture, histology of liver; treatment: tiazofurin; controlled by immunisation and mosquito control

Unclassified Flavivirus

Cacipacore virus: Japanese encephalitis serological complex; South America

Russian spring-summer encephalitis virus: tick vector; causes encephalitis, meningoencephalitis, hemorrhagic fever; Russian spring-summer encephalitis in former Soviet Union, Canada, USA

Yaounde virus: Japanese encephalitis serological complex; Africa

Hepacivirus

Hepatitis C virus: 35 nm; ssRNA; envelope; parenterally (including pooled plasma products; inactivated by severe terminal heat and solvent-detergent treatment, sporadic transmissions with pasteurisation) and sexually transmitted non-A, non-B hepatitis; causes hepatitis, hemorrhagic fever, 'influenza-like illness', infusion infection; chronicity (prolonged carrier state similar to hepatitis B virus exists in some patients; ? associated with hepatocellular carcinoma, splenetic lymphoma; incubation period $\leq$ 7 w (range 2-22 w); prevalence varies from $<$ 0.5% in Scandinavia to 8-14% in Egypt; serum autoantibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced; diagnosis: hemagglutination, ELISA, immunoblot, PCR

Pestivirus : $>$ 3 viruses of cattle and pigs; helical capsid symmetry, enveloped virion, cytoplasm site of capsid assembly, surface membrane site of nucleocapsid envelopment, ether sensitive; helical capsid occurs in animal and plant viruses, but not in animal DNA viruses; helical ribonucleoprotein under capsid is flexible; all animal viruses with helical nucleocapsids also have lipid-containing envelopes

Unclassified Flaviviridae

GB virus A: latent tamarin virus

Hepatitits GB virus B: definitely causes hepatitis in tamarins; may cause acute hepatitis in humans

GB virus C: causes acute and chronic hepatitis (mild) in humans; transmitted by heterosexual intercourse

Hepeviridae

Hepevirus: hepatitis E virus; major cause of enterically transmitted hepatitis in developing countries; no chronicity; diagnosis: enzyme immunoassay, Western blot assay

Order Nidovirales

Family Coronaviridae: single positive strand RNA, 50-160 nm diameter, molecular weight 5-6X10^6 D (18 kb), enveloped particle, spherical, pleomorphic, pedunculate, with petal-like or club-shaped surface projections; replicate in cytoplasm of infected cells; intracytoplasmic membranes site of nucleocapsid development; ether or chloroform inactivates; buds into cytoplasmic vacuoles

Coronavirus: human coronavirus; single strand RNA; envelope from infected cell; 2 types; survival time in water unknown (source human feces); causes common or feverish cold, URTI, acute chest infection, gastroenteritis, epidemic viral diarrhoea; infection generally confined to epithelial surface of respiratory tract; intestinal coronaviruses (described for pigs, foals, calves, sheep, dogs, mice, man and turkeys; maximum susceptibility in first few weeks of life) replicate in intestinal epithelium, producing lactose intolerance and diarrhoea; group includes mouse hepatitis virus (multiplies in macrophages), infectious bronchitis virus of fowl and $>$ 2 other agents infecting pigs and other vertebrates

Human torovirus: ? causes epidemic viral diarrhoea

Order Picornavirales

Family Picornaviridae: positive single strand RNA acts as messenger, translated monodirectionally into giant peptide, subsequently cleaved, no envelope from infected cell, molecular weight 2.3-2.6X10^6 D, in icosahedral, ether-resistant capsid with 32 capsomeres, 22-30 nm diameter; replicate in cytoplasm of infected cell; stabilised to heat at 50°C/1 h by 1M-$MgCl_2$; stable at acid pH; found in enteric tract and hence in sewage; penetrate host cells by endocytosis

Cardiovirus

Encephalomyocarditis virus: causes encephalomyocarditis; major host defence mechanism interference with adherence (++++)

Mengo encephalomyocarditis virus: causes non-pyogenic meningitis

Enterovirus: stable at pH 3.9, relatively unstable at 50°C, density 1.33-1.34 g/cm^3 in CsCl; increased infectiousness in abnormal host (clinical infection); enters across epithelial surface of intestinal tract and subsequently spreads through body;

immunity due to antibody (++), cell-mediated immunity (+); causes mild summer colds, rhinitis, croup, influenza-like illness, nonexudative pharyngitis and tonsillitis, otitis media, 70-79% of nonpyogenic meningitis (33% of syndromes), meningoencephalitis, 3-40% of encephalitis, neonatal disease, myocarditis, pericarditis, chronic infections in immunocompromised, poliomyelitis-like illness, hand-foot-and-mouth disease, ? acute infective lymphocytosis, ? diabetes type 1
Coxsackievirus: 24 coxsackievirus A, 6 coxsackievirus B; pathogenic for baby mice; survives 2 d - 46 w in water (source human feces); causes acute hemorrhagic conjunctivitis, common or feverish cold, diabetes, encephalitis, epidemic viral diarrhoea (A, B3), fever with exanthem, hand, foot and mouth syndrome, prenatal hepatitis, herpangia + exanthem, macular rash, maculopapular rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, anaphylactoid purpura, chronic or recurrent rash, nonpyogenic meningitis, mouth ulcers, myocarditis of newborn and interstitial myocarditis and valvulitis in infants and children, pancreatitis, parotitis and submandibular sialadenitis, pericarditis, epidemic pleurodynia, pneumonia with exanthem, acute paralytic poliomyelitis, febrile URTI in military recruits, febrile pharyngitis in children, nonexudative pharyngitis and tonsillitis, rhabdomyolysis, summer febrile illness, pneumonitis, orchitis, generalised disease of newborn infants, 5% of nosocomial diarrhoea; replicates in striated muscle and intestinal lymphoid tissue; ? biliary excretion of virus into intestine; recovery from primary infection due to antibody; serum autoantibodies against heart muscle in patients with acute myocarditis; diagnosis: ELISA
Human enterovirus A: causes epidemic viral diarrhoea, aseptic meningitis
Human coxsackievirus A2: no growth in cell cultures; causes maculopapular rash, nonpyogenic meningitis with exanthem, transient paralytic disease, herpangia, fever with exanthem, summer febrile illness, nonexudative pharyngitis and tonsillitis
Human coxsackievirs A3: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes herpangia, summer febrile illness
Human coxsackievirus A4: no growth in cell cultures; causes nonpyogenic meningitis, herpangia with exanthem, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), petechial or purpuric rash (anaphylactoid), acute paralytic poliomyelitis, fever with exanthem, summer febrile illness, nonexudative pharyngitis and tonsillitis
Human coxsackievirus A5: no growth in cell cultures; causes nonpyogenic meningitis, herpangia, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), summer febrile illness, nonexudative pharyngitis and tonsillitis
Human coxsackievirus A6: no growth in cell cultures; causes nonpyogenic meningitis, herpangia, roseola-like illness, summer febrile illness, nonexudative pharyngitis and tonsillitis, maculopapular rash
Human coxsackievirus A7: may grow in monkey kidney or HeLa cells; causes nonpyogenic meningitis with exanthem, paralytic disease (acute paralytic poliomyelitis), maculopapular rash, vesicular rash (hand, foot and mouth syndrome), pneumonia with exanthem, summer febrile illness
Human coxsackievirus A8: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes herpangia, vesicular rash, summer febrile illness, nonexudative pharyngitis and tonsillitis
Human coxsackievirus A10: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, herpangia, acute URTI (cold), maculopapular rash, vesicular rash (hand, foot and mouth syndrome), erythema multiforme or Stevens-Johnson syndrome, summer febrile illness, nonexudative pharyngitis and tonsillitis
Human coxsacievirus A12: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, summer febrile illness
Human coxsackievirus A14: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, summer febrile illness
Human coxsackievirus A16: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes nonpyogenic meningitis, herpangia, fever with exanthem, hand, foot and mouth syndrome, maculopapular rash, generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, chronic or recurrent rash, summer febrile illness
Human enterovirus 71: causes macular rash, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), nonpyogenic meningitis with exanthem
Human enterovirus B: grows well in primary monkey kidney, human diploid fibroblasts, Hep2, HeLa cells, 4 d to isolation, focal, swollen, glassy cells, detachment from glass (neutralisation test); causes pancreatitis, orchitis, perinatal generalised disease (myocarditis, hepatitis), pleurodynia ('Devil's grip'), aseptic meningitis
Echo 9 virus: 9% of nonpolio enterovirus isolates; causes nonpyogenic meningitis with exanthem (uncommon epidemic), epidemic viral diarrhoea, fever with rash (common epidemic), otitis media, paralysis (uncommon sporadic), pharyngitis in children, acute exudative tonsillitis, rash (maculopapular, vesicular, petechial or purpuric, roseola-like illness, anaphylactoid purpura), summer febrile illness, encephalitis, ataxia, pneumonia with exanthem
Human coxsackievirus A9: grows in monkey kidney and human amnion and embryonic kidney cells, may grow in HeLa cells; causes nonpyogenic meningitis with exanthem, paralytic disease (acute paralytic poliomyelitis), herpangia with exanthem, fever with exanthem, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), petechial or purpuric rash (anaphylactoid), generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, pneumonia with exanthem, pneumonitis, summer febrile illness, nonpurulent conjunctivitis

Human coxsackievirus B1: causes acute respiratory illness, pneumonia, prenatal hepatitis, nonpyogenic meningitis with exanthem, epidemic pleurodynia or myalgia, macular rash, maculopapular rash, vesicular rash (hand, foot and mouth syndrome), roseola-like illness, infectious myocarditis, infectious pericarditis

Human coxsackievirus B2: causes nonpyogenic meningitis with exanthem, acute URTI (cold), nonexudative pharyngitis and tonsillitis, epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, herpangia with exanthem, macular rash, maculopapular rash, vesicular rash, petechial or purpuric rash, roseola-like illness, orchitis, generalised disease of newborn infants, transient paralysis

Human coxsackievirus B3: causes nonpyogenic meningitis (most frequently reported enterovirus), transient paralytic disease, acute URTI (cold), summer febrile illness, epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, hand, foot and mouth syndrome, maculopapular rash, vesicular rash, petechial or purpuric rash, orchitis, generalised disease of newborn, summer febrile illness, nonexudative pharyngitis and tonsillitis (herpangia), epidemic viral diarrhoea

Human coxsackievirus B4: causes nonpyogenic meningitis with exanthem, paralytic disease, fever with exanthem, acute URTI (cold), epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, maculopapular rash, petechial or purpuric rash, generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, orchitis, generalised disease of newborn, summer febrile illness

Human coxsackievirus B5: causes nonpyogenic meningitis with exanthem, transient paralytic disease, acute URTI (cold), epidemic pleurodynia or myalgia, myocarditis of newborn, interstitial myocarditis and valvulitis in infants and children, pericarditis, orchitis, generalised disease of newborn, macular rash, maculopapular rash, vesicular rash (hand, foot and mouth disease), petechial or purpuric rash, generalised urticarial rash, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, onychomadesis and/or onycholysis, summer febrile illness, nonexudative pharyngitis and tonsillitis (herpangia)

Human coxsackievirus B6: causes nonpyogenic meningitis, summer febrile illness

Human echovirus 1: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis (uncommon sporadic; 3% of echoviral), maculopapular rash, paralysis (uncommon sporadic)

Human echovirus 2: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis (uncommon sporadic), exanthem (macular rash, maculopapular rash), paralysis (uncommon sporadic), encephalitis (uncommon sporadic), ataxia

Human echovirus 3: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis with exanthem (uncommon epidemic), maculopapular rash, petechial or purpuric rash, encephalitis (uncommon epidemic)

Human echovirus 4: causes nonpyogenic meningitis with exanthem (common epidemic; 6% of echoviral), summer febrile illness with rash (common epidemic), exanthem (macular rash, maculopapular rash, petechial or purpuric rash), paralysis (uncommon epidemic), encephalitis (uncommon sporadic), ataxia, acute URTI (uncommon sporadic), ? vaginitis

Human echovirus 5: causes nonpyogenic meningitis (uncommon sporadic), summer febrile illness with rash (uncommon sporadic), macular rash, maculopapular rash, zoster-like rash

Human echovirus 6: causes nonpyogenic meningitis with exanthem (common epidemic), paralysis (uncommon sporadic), summer febrile illness with rash (uncommon sporadic), exanthem (maculopapular rash, vesicular (zoster-like) rash, erythema multiforme or Stevens-Johnson syndrome), encephalitis (uncommon sporadic), ataxia, enteritis (common epidemic), perinatal hepatitis, pleurodynia (uncommon sporadic), myocarditis (uncommon sporadic)

Human echovirus 7: 15% of enterovirus isolates; causes nonpyogenic meningitis (52% of *human echovirus 7* infections; 21% of echoviral cases; common sporadic), upper respiratory tract disease (14%), encephalitis (9% of *human echovirus 7* infections, 9% of enteroviral encephalitis; uncommon sporadic), nonspecific febrile illness (7%), rash (maculopapular, petechial or purpuric; 2%), carditis (1%), paralysis (0.6%), epidemic viral diarrhoea

Human echovirus 8: 7% of nonpolio enterovirus isolates; causes acute URTI (uncommon sporadic), enteritis (uncommon sporadic)

Human echovirus 11: 14% of nonpolio enterovirus isolates; causes nonpyogenic meningitis with exanthem (46% of *human echovirus 11* infections; 38% of echoviral cases; common epidemic), epidemic viral diarrhoea (23%), encephalitis (15% of *human echovirus 11* infections, 15% of enteroviral cases), common cold (9%), nonspecific febrile illness (8%), rash (maculopapular, vesicular, urticarial, erythema multiforme or Stevens-Johnson syndrome, roseola-like illness, chronic or recurrent rash; 2%), pneumonia with exanthem (1%; uncommon sporadic), carditis (0.6%), paralysis (0.4%; uncommon sporadic), ataxia, perinatal hepatitis; diagnosis: PCR

Human echovirus 12: causes summer febrile illness, epidemic viral diarrhoea

Human echovirus 13: causes summer febrile illness, macular rash, maculopapular rash, nonpyogenic meningitis (uncommon sporadic), coryza, pharyngitis, bronchitis, broncholitis, poliomyelitis-like illness, diarrhoea with fever, encephalitis, enteroviral sepsis

Human echovirus 14: causes nonpyogenic meningitis with exanthem (uncommon sporadic), summer febrile illness, exanthem (macular rash, maculopapular rash), enteritis (uncommon epidemic viral diarrhoea, perinatal hepatitis)

Human echovirus 15: causes summer febrile illness, nonpyogenic meningitis (uncommon sporadic)

Human echovirus 16: causes nonpyogenic meningitis (uncommon epidemic), summer febrile illness with rash (uncommon epidemic), exanthem (maculopapular rash, roseola-like illness), paralysis (uncommon sporadic), encephalitis, ataxia, herpangia with exanthem

Human echovirus 17: causes summer febrile illness, nonpyogenic meningitis with exanthem (uncommon sporadic; 3% of echoviral), macular rash, maculopapular rash, vesicular rash, herpangia with exanthem, nonpurulent conjunctivitis

Human echovirus 18: causes summer febrile illness with rash (uncommon epidemic), nonpyogenic meningitis with exanthem (uncommon epidemic), exanthem (macular rash, maculopapular rash, anaphylactoid purpura), paralysis (uncommon sporadic), encephalitis (uncommon sporadic), ataxia, enteritis (uncommon epidemic viral diarrhoea), nonpurulent conjunctivitis

Human echovirus 19: causes summer febrile illness with rash (uncommon sporadic), nonpyogenic meningitis (uncommon epidemic), macular rash, maculopapular rash, encephalitis (uncommon sporadic), acute URTI (uncommon epidemic), enteritis (uncommon sporadic), myocarditis (uncommon sporadic), perinatal hepatitis

Human echovirus 20: causes summer febrile illness, acute URTI (common cold; common epidemic), nonpyogenic meningitis (uncommon sporadic), enteritis (uncommon sporadic)

Human echovirus 21: causes summer febrile illness, nonpyogenic meningitis (uncommon sporadic)

Human echovirus 24: 3% of echovirus isolates; 44% associated with nonpyogenic meningitis; also causes summer febrile illness, enteritis (uncommon sporadic)

Human echovirus 25: causes summer febrile illness, maculopapular rash, nonpyogenic meningitis with exanthem (uncommon sporadic; 3% of echoviral), hemangioma-like lesions, roseola-like illness, acute URTI (uncommon sporadic)

Human echovirus 26: causes summer febrile illness

Human echovirus 27: causes summer febrile illness, maculopapular rash, roseola-like illness

Human echovirus 29: causes summer febrile illness

Human echovirus 30: causes nonpyogenic meningitis with exanthem (third most frequently reported enterovirus; common epidemic), carditis, encephalitis, gastroenteritis, respiratory tract illness, summer febrile illness, paralysis (uncommon epidemic), ataxia, macular rash, maculopapular rash, roseola-like illness; 28% of nonpolio enterovirus isolates (40% of isolates from faeces or rectal swabs, 21% from CSF, 19% from throat swabs, 16% from tissues, 1% from nasopharynx, 1% from urine, 5% from other sources)

Human echovirus 31: causes summer febrile illness, nonpyogenic meningitis (uncommon sporadic)

Human echovirus 32: causes summer febrile illness, hemangioma-like lesions, enteritis (uncommon sporadic)

Human echovirus 33: causes maculopapular rash, nonpyogenic meningitis with exanthem

Human enterovirus C

Human coxsackievirus A1: no growth in cell cultures; causes herpangia, nonpyogenic meningitis, summer febrile illness

Human coxsackievirus A11: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

Human coxsackievirus A13: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

Human coxsackievirus A15: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

Human coxsackievirus A17: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

Human coxsackievirus A18: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes summer febrile illness

Human coxsackievirus A19: no growth in cell cultures; causes febrile summer illness

Human coxsackievirus A20: no growth in cell cultures; causes summer febrile illness

Human coxsackievirus A21: no growth in cell cultures; causes herpangia, acute URTI (common or feverish cold; febrile URTI in military recruits), summer febrile illness

Human coxsackievirus A22: no growth in cell cultures; causes herpangia, nonpyogenic meningitis, summer febrile illness

Human coxsackievirus A24: may grow in monkey kidney, HeLa, human amnion or embryonic kidney cells; causes acute hemorrhagic conjunctivitis, acute URTI (cold), summer febrile illness, Bornholm disease (pleurodynia)

Human entreovirus D

Enterovirus 70: causes nonpurulent conjunctivitis, acute hemorrhagic conjunctivitis

Poliovirus: molecular weight $2.5X10^6$ D, 7.5 kb/strand, 1 segment, positive polarity; 3 types; survives 2-130 d in water (source human feces); causes acute paralytic and bulbar poliomyelitis, carditis, encephalitis (infrequent in impaired cell-mediated immunity), epidemic viral diarrhoea (types 2 and 3), febrile illness, non-pyogenic meningitis, respiratory infection; replicates only in primates or primate-derived cell cultures; viral capsid protein reacts with specific receptor on susceptible tissue cell (eg., neurone); carried in blood free in plasma; replicates in striated muscle and intestinal lymphoid tissue;

disseminates to reticuloendothelial tissue (liver, spleen, lymph nodes, bone marrow) via blood; affects macrophage accessory function; ? biliary excretion of virus into intestine; immunity associated with high titres of type-specific neutralising IgA on mucosal surface; recovery from primary infection due to antibody; 5 genes; diagnosis: isolation primary method (primary monkey kidney +++, human diploid fibroblasts +++, Hep2 +++, 5 d to isolation; random, swollen, glassy cells, rapid progression and detachment of cells from glass; neutralisation test), antigen detection not available, serology not generally available (viral isolate required)

Hepatovirus

Human hepatitis A virus: virus 30 nm; ssDNA; no envelope; survives > 24 d in water (source human feces); causes infectious hepatitis (short incubation hepatitis; entero (fecal-oral) transmission and transmission by pooled plasma products (inactivated by severe terminal heat or pasteurisation, not by solvent-detergent treatment); incubation period 15-40 d; acute onset; fever common; autumn and winter; commonest in children and young adults), arthritis, hepatic granuloma, hemorrhagic fever, nonpyogenic meningitis, myocarditis and pericarditis; replicates in liver; biliary excretion of virus into intestine; increased infectiousness in abnormal host; serum antibodies against DNA, lymphocytes, immunoglobulin, smooth muscle, cytoskeleton and liver cell membrane produced; no chronicity; virus in feces and blood incubation period and acute phase; prophylactic value of γ-globulin (passive immunity); diagnosis: ELISA for hepatitis A IgM antibody + total hepatitis A antibody, immune adherence hemagglutination test for hepatitis A IgM antibody, seroconversion of hepatitis A IgG antibody, counterimmunoelectrophoresis, immune electron microscopy of stool, indirect fluorescent antibody titre, radioimmunoassay

Parechovirus

Human parechovirus 1: causes summer febrile illness, maculopapular rash, nonpyogenic meningitis (uncommon sporadic), acute URTI (uncommon sporadic), enteritis (uncommon sporadic)

Human parechovirus 2: causes summer febrile illness, nonpyogenic meningitis, enteritis (uncommon sporadic)

Rhinovirus: common cold virus; causes cold (++++), croup, febrile upper respiratory infection (++), otitis media, rhinitis, acute sinusitis, nonexudative pharyngitis and tonsillitis, clinical infection in abnormal host, asthma exacerbation; > 115 types infecting humans, 2 viruses of cattle; acid labile (unstable below pH 5-6), relatively stable at 50°C, density 1.38-1.41 g/cm^2 in CsCl; disease-producing dose in man: nasal cavity 1 TCID 50, conjunctiva 16 TCID 50, posterior pharyngeal wall 200 TCID 50; infection generally confined to epithelial surface of respiratory tract; replicates only in primates or in primate-derived cell cultures (primary monkey kidney +, human diploid fibroblasts +++, Hep2 negative; 7 d to isolation; focal, swollen or granular cells; pH 3 stability, neutralisation test); immunity is associated with high titre of type-specific neutralising IgA on mucosal surface

Family Togaviridae: positive single strand RNA (infectious), lipid envelope from infected cell; site of nucleocapsid envelopment surface membrane or intracytoplasmic membranes; ether sensitive; diameter of virion 20-70 nm, molecular weight of nucleic acid in virion 3-4.6X10^6 D, 12 kb; icosahedral symmetry; multiplies in arthropods; penetrates cell wall by endocytosis; 200 different types; unstable without added protein but survives several months at –20°C, indefinitely at –70°C or if lyophilised; hemagglutinates red blood cells from newborn chicks or geese; diagnosis: serology primary method (only primary togavirus infection of individuals not previously exposed to similar togavirus can be diagnosed reliably by rises in antibody titre), isolation not generally available (best animal host suckling mouse), antigen detection not available

Alphavirus: arbovirus group A; 23 members; 27-70 nm diameter, with 32 capsomeres in a lipid envelope; single stranded RNA, molecular weight 3X10^6 D; replicates in cytoplasm and matures by budding from surface membrane; causes Eastern equine encephalitis, Venezuelan equine encephalitis, Western equine encephalitis (includes Sindbis), Getah, Semliki; mosquito-borne; replicates in arthropods; adsorption by temperature-independent process, synthesis of large polypeptide cleaved to give structural polypeptides, attachment to inner surface of host cell membrane

Barmah Forest virus: mosquito vectors as for ***Ross River virus***; Australia (≈ 700 notified cases/y (55% in Queensland)); causes arthritis, arthralgia, rash, fever, lethargy, malaise

Eastern equine encephalitis virus: Atlantic and Gulf coasts of USA (freshwater swamps; ≈ 3 cases (2 deaths)/y), Canada, Brazil, Cuba, Panama, Philippines, Dominican Republic, Trinidad; reservoir wild birds; vector *Culex melanura* mosquito; causes encephalitis (summer and early autumn; ≈ 42-50% case-fatality rate)

SFV Complex

Chikungunya virus: mosquito vector; headache, fever (may be hemorrhagic), rash, joint and muscle pains; E Africa, S Africa, SE Asia

Mayaro virus: mosquito vector; headache, fever, joint and muscle pains; Bolivia, Brazil, Colombia, Trinidad

Ross River virus: mosquito vector (*Aedes vigilax* and *Aedes camptorhynchus* in salt marshes, *Culex annulirostris* in fresh water; also *Aedes normanensis, Coquillettidia linealis* and *Aedes notoscriptus*); Australia, New Guinea, Solomon Islands; causes Ross River fever, arthritis, 'influenza-like illness', macular rash; diagnosis: culture of serum, ELISA (IgG and IgM)

Semliki Forest virus: mosquito vector; fever or no symptoms; E Africa, W Africa

VEEV Complex

Venezuelan equine encephalitis virus: Central and S America (Brazil, Colombia, Ecuador, Trinidad, Venezuela, Mexico), southern USA (Florida, Texas); reservoir rodents and horses; vector *Culex* and other mosquitoes; also infectious as

aerosol and possible biowarfare agent (10-100 organisms required for infection); causes encephalitis (< 3 cases/y in USA; fatalities rare)

WEEV Complex

***Sindbis virus*:** mosquito vector; causes hemorrhagic fever but usually subclinical; ≈ 35 cases (< 1 death)/y; Egypt, India, S Africa, Australia

***Western equine encephalitis virus*:** freshwater swamps and irrigated areas west of Mississippi River, Canada, Mexico, Argentina, Brazil, British Guiana; reservoir wild birds, especially English sparrows; vector *Culisetta melanura* and *Culex tarsalis* mosquitos; causes Western equine encephalitis (summer and early autumn; ≈ 20 cases (mainly infants and children)/y; < 3% case-fatality rate)

Rubivirus

***Rubella virus*:** enveloped particle 60 nm diameter with 33 nm internal core of ribonucleoprotein; causes rubella (German measles), abortion, arthritis (usually adult women; fingers, wrists and knees), carpal tunnel syndrome (11% of total due to virus and 14% due to vaccine), catarrh, coryza, encephalitis (progressive rubella panencephalitis—slow viral disease), meningoencephalitis (rare), nonpyogenic meningitis, prenatal generalised disease (including hepatitis, urinary infection), stillbirth, teratogenic effects, Guillain-Barré syndrome, myocarditis and pericarditis, nonpurulent conjunctivitis, erythematous rash, maculopapular rash; increased infectiousness in abnormal host; infects lymphocytes and macrophages; chronic infection; immunity cell mediated (+++); diagnosis: negative passive hemagglutination with positive ELISA (IgG, IgM and IgM capture), hamagglutination inhibition (diagnostic titre ≥ 1:8), tissue culture of urine, throat swab, amniotic fluid, placenta

Subviral Agents: Satellites, Viroids and Prions

Prions: Spongiform Viral Encephalopathy Agents; increased infectiousness in abnormal host (clinical, ? subclinical, latent and persistent nonlatent infections)

Creutzfeldt-Jakob: slow agent distinct from conventional viruses; mean age at death 65 y, median duration of illness 4 mo, psychiatric presentations uncommon, typical periodicity on EEG seen in 65-70%, pulvinar sign on brain MRI scan in < 10%, prion protein plaques rare in brain, absent from tonsils

Kuru: slow agent distinct from conventional viruses; long incubation; lethal

Scrapie: slow agent distinct from conventional viruses; ? infects lymphoreticular tissues; no detectable antibody; mean doubling time 4-7 d in mouse brain

Bovine Spongiform Encephalopathy: causes 'mad cow disease' (200,000 cases in UK since 1986, due to contaminated feed), condition similar to Creutzfeld-Jakob disease in humans (> 80 cases in UK, 3 in France, 1 in Republic of Ireland; median age at death 29 y, median duration of illness 14 mo, psychiatric presentations very common, typical periodicity on EEG absent, pulvinar sign on brain MRI scan in > 70%, numerous florid prion protein plaques throughout the brain characteristic and also present in tonsils)

Situations in Which Viral Diagnosis Can Be Helpful: severe pneumonia unresponsive to antimicrobials and no bacterial etiology determined (*influenzavirus A*, adenovirus, *parainfluenza virus*, *respiratory syncytial virus*), myopericarditis (*coxsackievirus B*), acute gastroenteritis (*Rotavirus*—especially in infants and children), macular and maculopapular exanthems and enanthems (*human rubella virus, measles virus*, enteroviruses, adenovirus), vesicular exanthems and enanthems (*Simplexvirus* and *human herpesvirus 3*), congenital or perinatally acquired illness (*human cytomegalovirus*, *simplexvirus*, rubella, enteroviruses), febrile mononucleosis-like or sepsis-like syndromes (*Epstein-Barr virus*, *human cytomegalovirus*, adenovirus, enteroviruses), conjunctivitis and keratitis (adenovirus, *Simplexvirus*), hepatitis (hepatitis A, B, C, *human cytomegalovirus*, *Epstein-Barr virus*, adenovirus, *coxsackievirus B*)

Chapter 17

Bacteria

Superkingdom Bacteria
Phylum Actinobacteria
Class Actinobacteria: high G+C Gram positive bacteria
Subclass Actinobacteridae
Order Actinomycetales: Gram positive, some acid-fast, rods and filaments tending to branch; mostly nonmotile
Suborder Actinomycineae
Family Actinomycetaceae
Actinobaculum massiliae: isolated from urine of woman with recurrent cystitis
A.suis: usually grows on MacConkey; a clear zone of hemolysis produced by most strains; ferments glucose (no gas), xylose, lactose, sucrose, maltose and mannitol (variable); positive test reactions for indophenol oxidase, urease and esculin; usually produces catalase; commensal and pathogen of pigs, hamsters, donkeys, horses, cattle and zebras; isolated from animal-bite wounds of humans
Actinomyces: Gram positive irregular rods (some clubbed) and filaments, 0.5-2 μm diameter, branching (not always apparent), non-acid-fast, no spore formation; nonmotile; anaerobic or microaerophilic, growing better when CO_2 added to medium; may take 2 w or longer to grow in supplemented thioglycolate broth or on solid media (blood agar + vitamin K, colistin nalidixic acid agar); requires rich media (eg., blood or brain heart infusion); poor growth below 37°C; grows on agar as white, spherical or lobulated colonies; end-products of fermentation succinic and lactic acids with small amounts of acetic or formic acids (propionic acid not produced); usually catalase and indole negative; glucose fermented; forms granules in tissue; normal flora of mouth (usually present; oral cavity, dental plaque and calculus), tonsils (usually present), irregularly present in intestine; also animal; causes actinomycosis, abscesses (including hepatic, brain and epidural), acute dacrocystitis, adenitis and canaliculitis, adult hepatitis, hepatic granuloma, mycetoma, myocarditis and pericarditis (rare), parotitis and submandibular sialadenitis, salivary calculi, 44% of anaerobic dental infections, 32% of anaerobic CNS infections, 21% of anaerobic animal bite infections, 14% of transtracheal aspirates and pleural fluids growing anaerobes, 10% of anaerobic osteomyelitis; extracellular; diagnosis: Gram stain, direct immunofluorescent stain and anaerobic culture of pus, curettings, biopsy from wall of abscess; susceptible to penicillin (80%), di/flucloxacillin, amoxy/ampicillin, tetracyclines, erythromycin (100%), azithromycin, clarithromycin, roxithromycin, clindamycin (85%), lincomycin, chloramphenicol (98%), azlocillin (100%), piperacillin (100%), piperacillin-tazobactam, mezlocillin (100%), carbenicillin (100%), imipenem (100%), meropenem, ticarcillin-clavulanate (100%), vancomycin, teicoplanin; resistant to ciprofloxacin
A.bovis: cell wall lysine and aspartic acid; causes actinomycosis
A.israelii: cell wall lysine and ornithine; Gram positive branching filaments or diphtheroidal; microaerophilic or obligate anaerobe; requires rich media; rough colonies on blood agar, up to 1 mm diameter (often smaller), usually very raised or heaped in centre, usually whitish and either circular around to edge or irregular in outline (molar tooth colony), normally have glistening appearance under microscope; may appear dry but are usually moist when touched with a loop; granular or diffuse growth in enriched thioglycolate broth; usually associated with animals; normal flora of human mouth; causes actinomycosis (endogenous; progressive chronic inflammation with suppuration and formation of sinuses and sulphur granules; cervicofacial, abdominal, pulmonary, brain, bone, liver, kidney, female pelvic organs), bacteraemia and septicemia (usually in pulmonary actinomycosis), endometritis, infections in abnormal host, mycetoma, otitis externa (very rare), parametritis, pelvic abscess, pelvic inflammatory disease (almost exclusively associated with IUD), peritonitis, salpingitis; diagnosis: Gram stain and culture, direct immunofluorescence; treatment: penicillin ± streptomycin, tetracycline, erythromycin, cephalosporins
A.meyeri: cells diphtheroidal, branching; obligate or facultative anaerobe; smooth colonies on blood agar; diffuse growth in enriched thioglycoate broth; causes actinomycosis
A.naeslundii: possibly homologous with *A.viscosus*; cells diphtheroidal, branching; facultative anaerobe; smooth colonies on blood agar; diffuse growth in enriched thioglycolate broth; causes actinomycosis
A.odontolyticus: cells diphtheroidal, branching; microaerophilic or obligate anaerobe; usually red pigment on blood agar; colonies up to 5 mm diameter, regular and smooth with entire edge, centre slightly raised; diffuse growth in enriched thioglycolate broth; causes actinomycosis
A.viscosus: possibly homologous with *A.naeslundii*; cells diphtheroidal, branching; facultative anaerobe; small colonies on blood agar; diffuse growth in enriched thioglycolate broth
Arcanobacterium: facultatively anaerobic Gram positive short irregular rods, non acid-fast, nonmotile; usually catalase negative; human, animal

A.haemolyticum: β-haemolytic; catalase negative; morphology and most reactions similar to *C.diphtheriae* but poor growth on Tinsdale agar, lactose and gelatine negative; causes acute nonexudative pharyngitis and tonsillitis, chronic ulcers, septic arthritis; treatment: penicillin, erythromycin, rifampicin

A.pyogenes: cells diphtheroidal, coccoidal; facultative anaerobe; smooth colonies on blood agar; diffuse growth in enriched thioglycolate broth; gelatine positive; catalase negative; causes subacute localised infections in cattle, pigs, sheep, brain abscess, empyema, peritonsillar abscess, pharyngitis, septic arthritis, vulvovaginitis, ulcer and wound infections in man

Mobiluncus: motile, anaerobic vibrio-shaped Gram negative bacillus; found in vagina of 0-22% of women with vaginal discharge; ? causes vaginosis; treatment: metronidazole, tinidazole, nimorazole, clindamycin, Aci-Jel™

Suborder Corynebacterineae

Family Corynebacteriaceae

Corynebacterium: presence of ester-linked β-hydrogenated long chain fatty acids characteristic of group and of mycobacteria; Gram positive irregular rods in 'Chinese letters', some clubbed forms; few weakly acid-fast; usually nonmotile; aerobic and facultative anaerobic; β or γ hemolysis; catalase positive; no H_2S produced in triple sugar iron agar; bile esculin, NaCl, PYR and salicin negative; nitrate, glucose and mannitol; normal flora of mouth, nose (adherence to nasal mucosa +), large intestine, lower ileum, external genitalia, anterior urethra, vagina (37%), cervix (20-66%), skin, ear, eye; also animal, soil, plants; causes bacteraemia and septicemia, complication of cardiac surgery, endophthalmitis (postoperative), lung abscesses, perinatal generalised disease, 2% of endocarditis, infection in abnormal host (interrupted integument), systemic infections in granulocytopenics; growth stimulated by excess iron; treatment: penicillin ± aminoglycoside, erythromycin, vancomycin (resistance not yet reported); also susceptible to ofloxacin (MIC ≤ 0.25-1 mg/L), ciprofloxacin (0.25-1 mg/L)

C.bovis: γ-haemolytic, colonies white to cream, oxidase positive; causes infections in abnormal host, post-neonatal pyogenic meningitis (rare), otitis media (rare), chronic ulcers; treatment: erythromycin + rifampicin

C.diphtheriae: typical morphology in Gram stain (especially from Loeffler's slope); nonmotile; β-haemolytic; optimal growth on Loeffler's or Tinsdale medium; gravis type short, uniformly staining, low, circular colony; intermedius long, pleomorphic, clubbed, small colony; mitis long, pleomorphic, prominent granules, 'poached egg' colony; catalase, glucose, maltose and nitrate positive; VP, lactose and urease negative; sucrose and starch variable; important identification test agar gel diffusion; causes diphtheria (infection of nose, external mucosa of respiratory, auditory and genital tracts and, occasionally, skin; toxaemic diphtheria only if lysogenic), bronchitis, purulent conjunctivitis (uncommon), croup, endocarditis (nontoxigenic strains), nonexudative pharyngitis and tonsillitis, laryngotracheitis, myocarditis and pericarditis (usually following pharyngeal diphtheria), otitis externa (very rare), septic arthritis; natural host man; attaches to mucosal epithelium; infection generally confined to epithelial surface of respiratory tract; necrotising toxin (exotoxic protein), inhibits cell protein synthesis and oxidative processes, possibly through interference with cytochrome b, causing heart damage and nerve paralysis; isolates should be tested for toxin production; treatment: antitoxin + penicillin or erythromycin (resistance not yet confirmed in Australia), cefotaxime

C.equi: coryneform; grows well on ordinary media as large, irregular, highly mucoid, salmon-pink colonies; causes infections in abnormal host (opportunistic infection (diffuse interstitial pneumonia, pneumonitis, pulmonary abscess) associated with AIDS or T helper lymphocyte dysfunction and exposure to animals); treatment: rifampicin + erythromycin + surgery

C.jeikeium: glucose, galactose and catalase positive; urease negative; causes bacteraemia and septicemia (90% catheter-related), cellulitis (biopsy sites in granulocytopenic patients, endocarditis, localised skin lesions and local sepsis at sites of biopsy or catheter insertion or perianal fissure in granulocytopenic patients, peritonitis in continuous ambulatory peritoneal dialysis; susceptible to vancomycin (MIC ≤ 0.25 mg/L), teicoplanin (0.12-0.25 mg/L), sodium fusidate, rifampicin/rifabutin; usually resistant to β-lactams and aminoglycosides, erythromycin, clindamycin, imipenem; variable susceptibility to quinolones (susceptible to amifloxacin at 1 mg/L; resistant to ciprofloxacin)

C.kutscheri: causes chorioamnionitis, septic arthritis; treatment: ampicillin + gentamicin, cefotaxime, erythromycin

C.matruchotii: normal flora of tooth surface (dental plaque and calculus), gingiva; may possibly act as opportunistic pathogen

C.minutissimum: causes erythrasma (endogenous; scaly condition of axilla, groin and between toes; infection confined to stratum corneum); case of recurrent breast abscess described; treatment: erythromycin

C.pseudodiphthericum: does not show pleomorphism (cells regular, evenly stained except for transverse septum, frequently in parallel rows); nonmotile; nitrate, urease and catalase positive; inert towards carbohydrates; causes endocarditis, pneumonia (trauma and immunodeficient), acute tracheitis (1 case); treatment: ampicillin + gentamicin, vancomycin ± tobramycin

C.pseudotuberculosis: grows poorly on most media but well on Loeffler's medium, yellowish friable colonies; catalase, urease, glucose and maltose positive; lactose negative; causes lymph gland infection, caseous lymphadenitis in sheep, local lymphadenitis and eosinophilic pneumonia in man; treatment: erythromycin (250-500 mg orally 4 times daily (child: 30 mg/kg daily in 4 divided doses) or penicillin + surgical drainage or excision

C.renale: cells large, pleomorphic, with pointed ends

C.striatum: cells characteristically striated on Gram stain; nitrate, glucose and sucrose positive; urease, maltose, mannitol and xylose negative; causes chorioamnionitis (rare), pleuropulmonary infections, bacteraemia, infection of exit sites of central venous catheters, thrombophlebitis associated with central venous catheters (rare), conjunctivitis; treatment: vancomycin (MIC $\leq$ 0.25 mg/L); also susceptible to rifampicin ($\leq$ 0.008 mg/L), gentamicin ($\leq$ 1 mg/L)

C.ulcerans: morphology similar to *C.diphtheriae*; urease positive; nitrate negative; causes acute nonexudative pharyngitis and tonsillitis resembling diphtheria, and peritonsillar abscess; usually self-limiting but isolates should be tested for toxin production; from unpasteursied milk

C.urealyticum: urease, hippurate and catalase positive; glucose, galactose, PYR and ribose negative; causes wound infections, local and generalised sepsis, acute cystitis, bacteremia and septicemia in immunosuppressed; treatment: vancomycin (MIC 0.25-0.5 mg/L); also susceptible to teicoplanin (0.12-0.25 mg/L); usually resistant to β-lactams and aminoglycosides, varying susceptibility to quinolones

C.xerosis: nonmotile; colonies small, yellow to tan; catalase, nitrate, glucose and sucrose positive; maltose and starch negative; normal flora of eye; causes endocarditis (children and i.v. drug abusers with AIDS), septic arthritis following vascular surgery, infections in abnormal host; treatment: cefotaxime, erythromycin

Family Mycobacteriaceae

Mycobacterium: cells rods of variable length (coccoid to filaments), weakly Gram positive, strongly acid fast and acid/alcohol fast, not branching; meso-diaminopimelic acid, arabinose and galactose in cell wall; nonmotile; catalase positive; normal flora of large intestine, lower ileum, external genitalia, anterior urethra, vagina, skin; also animal, environment; causes bone marrow infection, 40% of carpal tunnel syndrome, encephalitis, hepatic granuloma, 36% of lymph gland infection, skin mycobacteriosis (including chronic ulcers), otitis externa (very rare), diffuse interstitial pneumonia, pulmonary abscess, pulmonary tuberculosis, prostatic abscess (rare), infections in abnormal host (T lymphocyte dysfunction), systemic infections in cell-mediated immunity disorders; growth stimulated by excess iron; cell wall component resists killing and digestion by phagocytes, unknown factor inhibits lysosomal fusion; cell-mediated immunity important in host defence; material responsible for adjunct activity of mycobacterial waxes D is thought to be N-acetylmuramyl dipeptide; treatment: streptomycin, paraaminosalicylic acid, ethionamide, cycloserine, viomycin, ethambutol, rifampicin, isoniazid, dapsone, pyrazinamide, capreomycin

M.abscessus: non-sterile water implicated in most outbreaks (following cardiac surgery, cosmetic surgery, podiatric procedures, invasive otologic procedure, dialysis, injection of unapproved alternative medication); in cystic fibrosis from unknown source

M.africanum: causes tuberculosis

M.asiaticum: photochromogen; slow growth rate; rarely causes disease in humans (disseminated mycobacteriosis in AIDS); 0.01% of *Mycobacterium* isolates; incidence 0.1/100 000

M.avium-intracellulare: Runyon group III (nonchromogen); slow growing; growth at 25°C and 42°C variable; some strains show light yellow pigment that intensifies with age; weak catalase positive at 25-37°C, positive at 68°C; nitrate, tween hydrolysis and urease negative; serotyping helpful; widely distributed in environment; often associated with disease; 17-30% of *Mycobacterium* isolates; 71% of isolates respiratory; incidence 3/100 000; causes acute diarrhoea and/or vomiting in AIDS, adult hepatitis, dissemination (frequent in AIDS), infections in abnormal host, 12% of lymph gland infection (frequent local lymphadenitis in children), musculoskeletal infections (bone and joint; infrequent), pancreatitis (14% of cases in AIDS), granulomatous prostatitis and seminal vesiculitis (rare), pulmonary tuberculosis (chronic cavitating lung disease in adults; frequent), skin and soft tissue infections (infrequent), urinary infection (rare cases in renal transplant recipients); diagnosis: Ziehl-Neelsen stain and culture of appropriate specimen; treatment: ethionamide, cycloserine, ethambutol, rifampicin, streptomycin, clofazimine, ansamycin, isoniazid, rifabutin, amikacin, ciprofloxacin, azithromycin, clarithromycin (4-6 in combination) $\pm$ surgery; resistant to ofloxacin

M.avium: pathogenic to rabbit and chick, sometimes mouse; causes mycobacteriosis (avian tuberculosis) clinically indistinguishable from pulmonary tuberculosis but primary focus lower gastrointestinal tract and acquired through gastrointestinal tract; extrapulmonary (including granulomatous synovitis) and disseminated forms reported; susceptible to interleukin-4, granulocyte macrophage colony stimulatory factor, macrophage colony stimulatory factor and tissue necrosis factor-activated macrophages; interferon-β and interleukin-2 also induce autoimmune activity; treatment: isoniazid + rifampicin + pyrazinamide

M.bovis: *Mycobacterium tuberculosis* complex; niacin and nitrate negative, no growth on Lowenstein-Jensen medium containing 2-thiophene-carboxylic acid hydrazide; pathogenic for guinea pig, rabbit and mouse; often associated with disease; 0.07% of *Mycobacterium* isolates; incidence 0.01/100 000; causes tuberculosis (respiratory, genitourinary, lymphatic, skeletal; disseminated in AIDS); enteric infection via milk; also, uncommon zoonotic transmission from seals, rhinoceros and elk; inhibits phagocytic degranulation; escapes from phagosome; susceptible to interferon-γ and interleukin-6 activated macrophages; tissue necrotic factor active in experimental infection; treatment: isoniazid + rifampicin + pyrazinamide $\pm$ ethambutol or streptomycin

M.chelonae: Runyon group IV (rapid grower; growth after 3 d); growth at 25°C and 37°C, no growth at 42°C; no pigment; strong catalase positive at 25-37°C, positive at 68°C; p-aminosalicylate and salicylate degraded; resistant to ethambutol; urease positive; nicotinamidase, tween hydrolysis and nitrate negative; glucose, mannose and trehalose used as carbon source; serine and ethanolamine used as source of both nitrogen and carbon; serotyping helpful; often associated with disease; 1% of *Mycobacterium* isolates; incidence 0.2/100 000; causes bacteraemia and septicemia (catheter related), disseminated disease (in AIDS and patients undergoing haemodialysis; infrequent), granulomatous synovitis, local infections after implantation of prosthetic devices (including endocarditis associated with prosthetic valve), infections in abnormal host, keratitis and iritis, lymphadenitis (infrequent), musculoskeletal infections (frequent), peritonitis in continuous ambulatory peritoneal dialysis, pulmonary tuberculosis (infrequent), skin and soft tissue infections including subcutaneous abscesses (following trauma; frequent), thyroiditis; treatment: clarithromycin, amikacin, erythromycin, sulphisoxazole, cefoxitin, tetracycline, cotrimoxazole, triple sulpha, sulphamethoxazole, doxycycline, sulphacetamide; resistant to ciprofloxacin, ofloxacin

M.flavescens: intermediate growth rate; growth at 25°C and 37°C, no growth at 42°C; pigmented; strong catalase positive at 25-37°C, positive at 68°C; nitrate and tween hydrolysis positive; growth in 5% NaCl; urease negative; rarely associated with disease; 0.8% of *Mycobacterium* isolates; incidence 0.2/100 000

M.fortuitum subspecies fortuitum: Runyon group IV (rapid grower); growth at 25°C and 37°C, no growth at 42°C; no pigment; strong catalase positive at 25-37°C, positive at 68°C; urease, nitrate reduction and iron uptake positive; tween hydrolysis variable; serotyping helpful; 4-8% of *Mycobacterium* isolates; 40% of isolates from peritoneal fluid; incidence 0.7/100 000; cutaneous and ocular (keratitis and iritis) disease following trauma reported; causes local infections associated with implanted prosthetic devices, augmentation mammoplasty infection, bacteraemia and septicemia (catheter related), cellulitis, cervical lymphadenitis (infrequent), disseminated disease (infrequent; in AIDS and non-AIDS patients), infection in abnormal host, musculoskeletal infections (frequent), osteomyelitis and osteochondritis, peritonitis in continuous ambulatory peritoneal dialysis, prosthetic valve endocarditis, pulmonary tuberculosis (infrequent), skin and soft tissue infections (frequent), lupus vulgaris-like lesions; treatment: triple sulpha, amikacin (100% susceptible), cefoxitin (64% susceptible), tetracycline, erythromycin, cotrimoxazole, sulphamethoxazole (88% susceptible), doxycycline (91% susceptible), sulphisoxazole, sulphacetamide; also susceptible to ciprofloxacin (100% susceptible at 0.25 mg/L), ofloxacin (0.4 mg/L), norfloxacin (0.8 mg/L), clarithromycin (90% susceptible), imipenem (91% susceptible)

M.gastri: slow growth rate; growth at 25°C and 37°C, no growth at 42°C; no pigment; weak catalase positive at 25-37°C, negative at 68°C; tween hydrolysis and urease positive; nitrate negative; serotyping helpful; rarely associated with disease; 0.3% of *Mycobacterium* isolates; incidence 0.1/100 000

M.gordonae: slow growth rate; scotochromogen; small yellow-orange colonies in 2-6 w; growth at 25°C and 37°C, no growth at 42°C; strong catalase positive at 25-37°C, positive at 68°C; tween hydrolysis positive; nitrate and urease negative; uses glucose and n-butanol as carbon source; normal inhabitant of tap water; rarely associated with disease; causes granulomatous synovitis, disseminated mycobacteriosis in non-AIDS patients, occasional infections of respiratory tract and spleen in AIDS; 5-15% of *Mycobacterium* isolates; 42% of isolates from urine; incidence 3/100 000; treatment: isoniazid + rifampicin + pyrazinamide

M.haemophilum: nonchromogen; slow growing; potentially pathogenic in humans; causes disseminated mycobacteriosis in AIDS, skin and soft tissue infections (frequent), local and generalised sepsis (in immunocompetent), lymphadenitis (infrequent); treatment: rifampicin, isoniazid, ethambutol ± surgery

M.intracellulare: causes chronic mycobacteriosis (Battey disease) clinically indistinguishable from pulmonary tuberculosis; acquired by respiratory route; rare instances of lymphadenitis, osteomyelitis, renal abscess, thyroiditis and disseminated disease reported; susceptible to interferon-γ-activated macrophages

M.kansasii: Runyon group I (photochromogen); growth at 25°C and 37°C, no growth at 42°C; strong catalase positive at 25-37°C, positive at 68°C; nitrate reduced, tween hydrolysis and urease positive; serotyping helpful; pathogenicity for mouse variable; often associated with disease but not commonly found in environment; 3-5% of *Mycobacterium* isolates; 75% of isolates from respiratory; incidence 0.5/100 000; causes bone marrow infection, disseminated disease (infrequent; in AIDS), granulomatous synovitis, infections in abnormal host, lymph gland infection (local lymphadenitis in children; infrequent), musculoskeletal infection (bone, joint, bursitis; infrequent), pulmonary tuberculosis (chronic cavitating lung disease in adults; frequent), skin and soft tissue infection (sporotrichoidal, cutaneous 'tuberculosis', deep heel infection; infrequent); diagnosis: Ziehl-Neelsen stain and culture of appropriate specimen; treatment: rifampicin + isoniazid + pyrazinamide ± ethambutol, streptomycin, sulphamethoxazole, amikacin ± surgery; resistant to ciprofloxacin

M.leprae: obligate parasite of man but ? recoverable from soil, water, vegetation; attacks skin, nasal mucosa and nerves; causes leprosy (15 M lepers in world), adult hepatitis and hepatic granuloma (in 90% of lepromatous, and 20% of tuberculoid, cases); inhibits phagocytic microbicidal activity by resistance to granule substance; multiplies in macrophages; carried in blood associated with mononuclear cells; in lepromatous leprosy, immune complexes prominent in pathogenesis of clinical disease, cell-mediated immunity suppressed; recovery from infection and resistance to reinfection due to cell-mediated immunity; mean doubling time 2 w in vivo; diagnosis: modified Ziehl-Neelsen stain of scrapings from mucosal ulcers, fluid

from nodules, biopsy of macule, muscle or nerve, histology of biopsy, ELISA; treatment: dapsone + isoniazid, sulphonamides, rifampicin, clofazimine, ethionamide, prothionamide

M.lepraemurium: inhibits phagocytic microbicidal activity by resistance to granule substance (lysosomal enzymes)

M.malmoense: nonchromogen; slow growing; strict or potential pathogen; 0.03% of *Mycobacterium* isolates; incidence < 0.1/100 000; causes disseminated mycobacteriosis in AIDS and non-AIDS patients, lymphadenitis (infrequent), pulmonary infection (frequent); treatment: rifampicin, streptomycin, ethionamide, capreomycin, ethambutol, rifabutin, clofazimine, isoniazid ± surgery

M.marinum: Runyon group I (photochromogen); growth at 25°C, growth at 37°C variable, no growth at 42°C; weak catalase positive at 25-37°C, positive at 68°C; tween hydrolysis and urease positive; nitrate negative; does not use glucose or n-butanol as carbon source; pathogenic to mouse (local areas); 'indigenous' in sea water; often associated with disease; causes bursitis, granulomatous synovitis, musculoskeletal infections (frequent), skin and soft tissue infections (sporotrichoidal; frequent), swimming pool granuloma; 0.4% of *Mycobacterium* isolates; incidence 0.04/100 000; treatment: rifampicin, ethambutol, tetracycline, isoniazid, pyrazinamide ± surgery

M.microti: causes rodent tuberculosis; inhibits phagocytic degranulation

M.nonchromogenicum: growth at 42°C; slow growth rate (no growth after 3 d); p-aminosalicylate and salicylate not degraded; susceptible to ethambutol; nicotinamidase and tween hydrolysis positive; urease negative; glucose, mannose and trehalose not used as carbon source; serine and ethanolamine not used as source of both nitrogen and carbon; rarely causes disease in humans (chronic tenosynovitis of knee); treatment: ethambutol, sulphonamides, cotrimoxazole, erythromycin, streptomycin + surgical debridement

M.parafortuitum: rapid growth rate; usually non-pathogenic

M.paratuberculosis: slow growth rate; causes Johne's disease in animals, ? Crohn's disease in humans; survives normal pasteurisation

M.phlei: rapid growth rate; rarely associated with disease

M.scrofulaceum: Runyon group II (scotochromogen); growth at 25°C and 37°C, no growth at 42°C; strong catalase positive at 25-37°C, positive at 68°C ; urease positive; tween hydrolysis and nitrate negative; serotyping helpful; not pathogenic to animals; often associated with disease; 2% of *Mycobacterium* isolates; 50% of isolates from respiratory, 50% from urine; incidence 0.4/100 000; causes bone disease (rare), cutaneous ulcers (rare), disseminated infection (infrequent; in AIDS), infection in abnormal host, cervical lymphadenitis (frequent in children), pulmonary infection (chronic cavitating lung disease in adults; infrequent); usually resistant to drugs, requiring combination of isoniazid, streptomycin and cycloserine + surgery

M.simiae: photochromogen; growth at 25-37°C, variable growth at 42°C; strong catalase positive at 25-37°C, positive at 68°C; urease positive; nitrate and tween hydrolysis negative; serotyping helpful; often associated with disease but not commonly found in environment; 0.2% of *Mycobacterium* isolates; incidence 0.02/100 000; causes disseminated disease (infrequent), osteomyelitis (infrequent), pulmonary infections (chronic cavitating lung disease in adults; frequent); usually resistant to drugs, requiring combination of isoniazid, ethambutol and rifampicin

M.smegmatis: rapid growth rate; growth at 25°C, 37°C and 43-45°C; late-developing yellow to orange pigment in 50%; low semiquantitative catalase test, strong catalase positive at 25-37°C, positive at 68°C; tween hydrolysis and urease positive; serotyping not helpful; causes skin and soft tissue infections (primary and post-surgical (especially cardiac), catheter tunnel), cellulitis, local and generalised sepsis, disseminated mycobacteriosis in AIDS; treatment: sulphamethoxazole, amikacin, cefoxitin, doxycycline + surgery

M.szulgai: growth at 25°C and 37°C, variable growth at 42°C; scotochromogenic at 37°C and variably photochromogenic at 25°C; strong catalase positive at 25-37°C, positive at 68°C; nitrate and urease positive; tween hydrolysis variable; serotyping helpful; often associated with disease but not commonly found in environment; 0.1% of *Mycobacterium* isolates; incidence 0.03/100 000; causes disseminated disease (infrequent; in AIDS), musculoskeletal infection (bursitis; infrequent), pulmonary tuberculosis (chronic cavitating lung disease in adults, pneumonitis; frequent); treatment: rifampicin + isoniazid + ethambutol + ethionamide or cycloserine or streptomycin

M.terrae/M.triviale: growth at 25°C and 37°C, no growth at 42°C; slow growth rate; no pigment; strong catalase positive at 25-37°C, negative at 68°C; nitrate and tween hydrolysis positive; urease negative; serotyping helpful; rarely associated with disease; 2% of *Mycobacterium* isolates; 67% of isolates from respiratory; incidence 0.4/100 000

M.thermoresistibile: rapid growth rate; rarely causes disease in humans (2 pulmonary cases, 1 cutaneous)

M.tuberculosis: niacin and nitrate positive; growth on Lowenstein-Jensen medium containing 2-thiophene-carboxylic acid hydrazide; pathogenic for guinea pig and mouse; often associated with disease; 52% of *Mycobacterium* isolates; causes tuberculosis, chronic respiratory infection in man (10-15 M active cases in world), anterior uveitis, septic arthritis, bone marrow infection, brain abscess, 21% of carpal tunnel syndrome, cholangitis and cholecystitis, chorioretinitis, purulent conjunctivitis, acute diarrhoea and vomiting in AIDS, acute epididymitis and epididymoorchitis, erythema nodosum, adult hepatitis, 20% of hepatic granuloma, 20% of lymph gland infection, non-pyogenic meningitis, mesenteric lymphadenitis, mouth

lesions, mycotic aneurism, oesophagitis, 1% of osteomyelitis and osteochondritis, otitis externa (very rare), chronic draining otitis media, parotitis and submandibular sialadenitis, peritonitis (primary), pneumonia, psoas abscess, pulmonary abscess, septic arthritis, splenic abscess in AIDS, granulomatous synovitis, thyroiditis, infections in abnormal host, disseminated mycobacteriosis in AIDS; inhalation infectious dose in man 1-10 bacteria; exposure to ultraviolet light and particle size are responsible for secondary aerosols being less dangerous in transmission of tuberculosis than primary aerosols; enters across respiratory tract epithelial surface and subsequently spreads through body; inhibits phagocyte chemotaxis, lysosome-phagosome fusion (by bacterial sulphatide), degranulation, microbicidal activity (by resistance to granule substance); basic factors in pathogenesis of pulmonary tuberculosis include intracellular multiplication and delayed hypersensitivity; multiples in macrophages; cord factor virulence factor; primary immune defence activation of macrophages, by T cell-generated lymphokines (tissue necrosis factor, interferon-γ), rendering them resistant to infection (+++), killing of infected phagocyte also important; recovery from primary infection, resistance to reinfection and resistance to reactivation of latent infection due to cell-mediated immunity; cell-mediated immunity in tuberculosis has been called a 'double-edge sword' because it limits intracellular multiplication and mediates delayed hypersensitivity simultaneously; persists in lung or lymph node (infectious, shed to exterior), activation giving tuberculosis in middle aged; mean doubling time 24 h in vitro; diagnosis: auramine rhodamine stain of sputum or bone marrow, acid-fast smear, culture, tuberculin test, interferon gamma test, PCR (not faeces, synovial fluid or urine), DNA probe, gene amplification and hybridisation, ELISA; treatment: streptomycin (6.8% resistance in Australia), paraaminosalicylic acid, isoniazid (8.5% resistance in Australia), rifampicin (1.5% resistance in Australia), ethambutol (0.3% resistance in Australia), pyrazinamide, thiacetazone; susceptible to ciprofloxacin (MIC 0.5-1 mg/L), ofloxacin (0.8-1 mg/L)

M.ulcerans: nonchromogen; slow growing; often associated with disease but not commonly found in environment; causes chronic ulcers (Bairnsdale (Buruli) ulcer); treatment; streptomycin, dapsone, ethambutol, rifampicin + surgery, local heat

M.vaccae: rapid growth rate; usually nonpathogenic

M.xenopi: Runyon group III (nonchromogen); slowly produces small yellow colonies; grows best at 42°C; no growth at 25°C, growth at 37°C; weak catalase positive at 25-37°C, positive at 68°C; nitrate, tween hydrolysis and urease negative; pathogenicity for mouse and chick variable; often associated with disease; 0.2% of *Mycobacterium* isolates; causes disseminated disease (infrequent; in AIDS), pulmonary tuberculosis (chronic cavitating lung disease in adults, pneumonitis; frequent); incidence 0.03/100 000; treatment: isoniazid + rifampicin + pyrazinamide $\pm$ streptomycin or ethambutol $\pm$ surgery

Family Nocardiaceae

Nocardia: cells branched filaments $\rightarrow$ rods $\rightarrow$ cocci, some forming conidia on aerial hyphae; weakly acid-fast, variably Gram positive; nonmotile; mycolic acids present; meso-diaminopimelic acid, arabinose and galactose in cell wall; grows only aerobically, appearing in 2-5 d on blood and chocolated blood agar as rough, dry, velvety colonies digging into the agar; optimum growth at 5-10% CO_2 and 37°C; grows on simple media and at wide temperature range; catalase and urease positive; causes abscesses (including silent brain abscesses), chorioreitinitis, adult hepatitis, hepatic granuloma, postneonatal pyogenic meningitis, actinomycetoma, disseminated infection in cell-mediated immunity disorders; primary bodily defence mechanism leucocyte bactericidal function; diagnosis: Gram, Ziehl-Neelsen stain and culture of sputum, thoracentesis specimen, transtracheal aspirate, bronchial washings, lung biopsy, pus from abscess or draining sinus, biopsy from other affected sites, serology (immunodiffusion); susceptible to sulphonamides, trimethoprim, cotrimoxazole, minocycline, amikacin, imipenem

N.asteroides: Gram positive branching filaments, partially acid fast; starch not hydrolysed, casein, tyrosine, gelatine, acetamide and aryl negative; 36% of *Nocardia* isolates in Australia; causes abscesses without granules in mouse and guinea pig, frequently causes death; causes intense suppuration with minimal fibrosis; causes brain abscess in impaired cell-mediated immunity, postneonatal pyogenic and nonpyogenic meningitis (common in impaired cell-mediated immunity; case-fatality rate 57%), mycetoma, osteomyelitis and osteochondritis, diffuse interstitial pneumonia in T cell deficiency, pneumonitis in immunodeficient, infections in abnormal host (especially in alveolar proteinosis, Hodgkin's disease, immunosuppressive therapy, T lymphocyte dysfunction); immunity cell-mediated (delayed type hypersensitivity +++); diagnosis: immunodiffusion (antigen), Gram and acid-fast smears, culture (mycobacterial media, modified Thayer-Martin medium, paraffin-containing medium, BMPAα, MWY charcoal yeast extract agar); treatment: amikacin, sulphonamide, cotrimoxazole + streptomycin, minocycline, imipenem; also susceptible to tobramycin; resistant to erythromycin

N.brasiliensis: partially acid fast; starch not hydrolysed, casein, tyrosine and gelatine positive; abscesses with granules caused in mouse and guinea pig by some strains; causes 14% of nocardiosis in Australia (most common cause of lymphocutaneous), mycetoma, infections in abnormal host; treatment: cotrimoxazole or sulphamethoxazole + amikacin

N.brevicatena: acid-fast spores; trehalose positive, lysosome sensitive; relatively rare but generally associated with severe disease (pulmonary, brain, blood); treatment: cotrimoxazole, ciprofloxacin, cefotaxime, amikacin, minocycline, imipenem; also susceptible to tobramycin, sulphafurazole, cephamandole; resistant to erythromycin, augmentin

N.farcinica: growth at 45°C, acetamide and rhamnose positive, aryl negative; 17% of *Nocardia* isolates in Australia; sensitive to ciprofloxacin, augmentin; resistant to cefamandole, cefotaxime, erythromycin, ampicillin, tobramycin

N.nova: no growth at 45°C, aryl positive, acetamide and rhamnose negative; 25% of *Nocardia* isolates in Australia; causes peritonitis, abscesses; sensitive to cefamandole, cefotaxime, ampicillin, erythromycin; resistant to tobramcyin, ciprofloxacin, augmentin

N.otitdiscaviarum: 3% of *Nocardia* isolates in Australia; causes mycetoma; treatment: cotrimoxazole + amikacin

N.transvaliensis: 6% of *Nocardia* isolates in Australia

Rhodococcus: Gram positive rods, cocci, filaments, weakly acid fast; mycolic acids present; nonmotile; conidia not formed; catalase positive; humans, soil; susceptible to ciprofloxacin (MIC 1 mg/L)

Tsukamurella: Gram positive bacilli; identification requires high performance liquid chromatography, 16S ribosomal gene sequencing and DNA-DNA dot blots; cause bacteremia in immunosuppresssed patients with indwelling central venous catheters

Suborder Micrococcineae

Family Brevibacteriaceae

Brevibacterium casei: obligately aerobic gram positive bacilli associated with milk products and on human skin; causes bacteremia and sepsis associated with Hickmann catheter in AIDS patients

Family Cellulomonadaceae

Oerskovia: Gram positive, extensive branching → rods due to fragmentation → motile coccoid elements; facultative anaerobe; aerial mycelium not produced; non-acid fast; nitrate, gelatine, esculin, glucose, maltose and sucrose positive; urea, mannitol and xylose negative; catalase positive on aerobic incubation, negative if grown anaerobically; soil, clinical; causes bacteremia (catheter related), endocarditis (prosthetic valves); sometimes isolated from CSF but pathogenicity uncertain; treatment: ampicillin + cotrimoxazole; susceptible to metronidazole

Tropheryma whippelii: causes Whipple's disease, endocarditis; diagnosis: PCR on tissue, CSF, blood; small bowel biopsy

Family Dermatophilaceae

Dermatophilus: Gram positive filaments, branch at right angles, produce motile coccoid forms; substrate mycelium; non-acid fast; catalase positive; causes human and animal skin lesions

D.congolensis: causes dermatophilosis; diagnosis: Giemsa stain and culture of scabs and exudates

Family Intrasporangiaceae

Intrasporangium: aerial mycelium not produced

Family Microbacteriaceae

Leifsonia aquatica: motile at 35°C and 25°C; catalase positive; VP negative; oxidative; reported from blood cultures, endocarditis and neonatal meningitis

Family Micrococcaceae: Gram positive, may be encapsulated, form chains in liquid media, possess catalase, produce penicillinase

Kocuria kristinae: anaerobic acid production from glucose

Micrococcus varians: anaerobic acid production from glucose

Micrococcus: Gram positive cocci, cells round, single and in irregular clusters and tetrads, no capsule; no cell wall teichoic acid, no pentaglycine cross bridge in peptidoglycan; usually no anaerobic growth in glucose, growth in 5% NaCl, growth on furoxone-Tween 80-oil red agar; yellow pigmented strains, non-adherent to blood agar, nonhemolytic, large colonies; glucose oxidised; no anaerobic acid production from glycerol in presence of erythromycin; susceptible to 0.04 U bacitracin, susceptible to lysozyme (50μg), resistant to lysostaphin; DNA base composition 66-75% G+C; normal flora of skin, mouth, tonsils; normal habitat water; causes cat and dog bite infections, rare cause of endocarditis; treatment: vancomycin (< 5% resistance in Australia)

M.luteus: adherence to nasal mucosa+; inhibits phagocytic microbicidal activity by resistance to oxidative attack; susceptible to gentamicin

Rothia: Gram positive filaments, rods, cocci, clubbed forms, non acid-fast; nonmotile; catalase positive; indole negative; oral cavity

R.dentocariosa: normal flora of mouth (dental plaque and calculus); may on occasion act as opportunistic pathogen, causing mouth abscesses, infections in abnormal host, subacute bacterial endocarditis (rare; i.v. drug abusers, poor dentition, congenital heart disease); treatment: penicillin, amoxycillin or vancomycin + gentamicin or netilmicin

R.mucilaginosa: capsule present; cells in clusters; large colonies, adheres to blood agar, nonhaemolytic; no growth in 5% NaCl, anaerobic growth in glucose; catalase variable; normal flora of mouth and upper respiratory tract; causes bacteraemia and septicemia and endocarditis (i.v. drug abuse, cardiac valve disease, vascular catheters, immunocompromised), peritonitis in chronic ambulatory peritoneal dialysis; treatment: vancomycin (100% susceptible), gentamicin (100% susceptible), penicillin (71% susceptible)

Suborder Micromonosporineae

Family Micromonsporaceae

Actinoplanes: meso-diaminopimelic acid and glycine in cell wall

Suborder Propionibacterineae

Family Propionibacteriaceae

Propionibacterium: Gram positive irregular rods, diphtheroids, branched, coccoid, non-acid-fast, nonsporeforming; nonmotile; microaerophilic or anaerobic; smooth colonies on blood agar; glucose fermented, propionic and acetic acids major end-products of fermentation; usually catalase positive; indole positive; normal flora of upper respiratory tract (usually present), mouth (irregular), skin (large numbers), colon (irregular), vagina (usually present); also dairy; causes brain abscess, cerebrospinal fluid shunt infections, endocarditis, chronic mastitis and breast abscess, osteomyelitis and osteochondritis, peritonsillar abscess, pulmonary abscess; susceptible to penicillin, amoxy/ampicillin, amoxycillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, cephalexin, cephalothin, cephazolin, cefaclor, cefuroxime, cefotaxime, ceftriaxone, cefepime, cefpirome, ceftazidime, cefotetan, cefoxitin, metronidazole, chloramphenicol, vancomycin, teicoplanin, clindamycin/lincomycin (100% susceptible), imipenem (100%), meropenem, azithromycin, clarithromycin, erythromycin, roxithromycin

P.acnes: obligate or facultative anaerobe; diffuse (granular) growth in enriched thioglycolate broth; catalase and indole variable; metabolic products acetic, propionic, lactic and succinic acids; normal flora of nose, skin, mouth; may contribute to lesions of acne vulgaris (endogenous); causes bacteraemia (colonising prostheses), endocarditis, infections in abnormal host, late infections after hip-joint surgery, chronic otitis externa, splenic abscess, 37% of anaerobic CNS infections, 33% of anaerobic animal bite infections, 16% of anaerobic osteomyelitis; treatment: penicillin; also susceptible to meropenem (MIC 0.25 mg/L), ticarcillin ($\leq$ 1 mg/L), ticarcillin-clavulanate ($\leq$ 1 mg/L), imipenem (100%), clindamycin (100%)

P.avidum: facultatively anaerobic; diffuse growth in enriched thioglycolate broth; catalase positive; indole negative; metabolic products acetic, propionic and succinic acids, with small amount of lactic acid; normal flora of skin, intestines; causes splenic abscess; treatment: penicillin; also susceptible to meropenem (MIC 0.25 mg/L)

P.granulosum: facultatively anaerobic; diffuse growth in enriched thioglycolate broth; catalase positive; indole negative; metabolic products acetic, propionic and succinic acids, with small amount of lactic acid; susceptible to meropenem (MIC 0.25 mg/L)

P.propionicum: cells branching filaments or diphtheroidal; microaerophilic or obligate anaerobe; rough colonies on blood agar; growth in enriched thioglycolate broth granular or diffuse; catalase and indole negative; glucose fermented; metabolic products acetic and propionic acids, with small amounts of lactic and succinic acids; normal flora of mouth (oral cavity, dental plaque), tonsillar crypts; on occasion, produces chronic abscesses and draining sinuses; causes actinomycosis, acute dacrocystitis, adenitis and canaliculitis and dacryocystitis (particularly older males); treatment: penicillin, tetracycline, erythromycin

Suborder Pseudonocardineae

Family Pseudonocardaceae

Saccharopolyspora rectivirgula: causes bagassosis and farmer's lung

Suborder Streptomycineae

Family Streptomycetaceae

Streptomyces: cells branching, filaments, Gram positive, non-acid fast, mycelium formed, little fragmentation, usually with conidia on aerial hyphae forming chains; arthrospores; L-diaminopimelic acid and glycine in cell wall; nonmotile; colonies tough; no anaerobic growth; urease, arabinose and xylose negative; causes mycetoma

S.griseus: isolated from sputum (36%), wound (32%), blood (25%), brain (7%); susceptible to amikacin

S.paraguayensis: causes mycetoma; treatment: cotrimoxazole + amikacin

S.ricefensis: causes mycetoma

S.somaliensis: causes mycetoma; treatment: cotrimoxazole + amikacin

Suborder Streptosporangineae

Family Nocardiopsaceae

Nocardiopsis dassonvillei: has been isolated from clinical specimens but its role as a human pathogen is uncertain

Family Thermonosporaceae

Actinomadura: delicate, non-fragmenting, branched filaments, non-acid fast; meso-diaminopimelic acid in cell wall; aerobic; growth in simple media; usually found in soil

A.madurae: not acid fast; arthrospores; arabinose and xylose positive, casein and starch hydrolysed; urease negative; not pathogenic to mice and guinea pig; causes mycetoma; treatment: cotrimoxazole + amikacin; also susceptible to ceftriaxone, imipenem

A.pelletierii: not acid fast; urease, arabinose and xylose negative; casein hydrolysed, starch not hydrolysed; not pathogenic to mice and guinea pig; causes mycetoma; treatment: cotrimoxazole + amikacin

Order Bifidobacteriales

Family Bifidobacteriaceae

Bifidobacterium: Gram positive rod, irregular, branching, nonsporeforming; nonmotile; obligately anaerobic; major end-products of fermentation acetic acid and lactic acids $\pm$ formic acid (propionic and butyric acids not formed); catalase

positive; normal flora of mouth (usually present), large intestine (large numbers), vagina (irregular); also sewage; causes actinomycosis, diverticulitis, peritonitis; treatment: tetracycline, penicillin, erythromycin; also susceptible to meropenem (MIC 1 mg/L)

B.adolescentis: normal flora of oral cavity, tonsils and intestinal tract; has caused lung abscesses and pleural fluid

B.animalis: used as probiotic

B.breve: used as probiotic

B.dentium: thin rods, bifid or bulbous ends; obligate anaerobe; smooth colonies on blood agar; diffuse growth in enriched thioglycolate broth; catalase and indole negative; glucose fermented, metabolic products acetic and lactic acids; has been isolated from human tissues but role as pathogen not clear

B.longum: used as probiotic

Gardnerella vaginalis: Gram variable diphtheroid-like, irregular or pleomorphic rods, non-acid-fast, asporogenous; nonmotile; aerobic and facultatively anaerobic; CO_2 required; fastidious; γ-haemolytic on horse blood agar, β-haemolytic on sheep blood agar (minute colonies), wide (sometimes double) zone of incomplete β-like haemolysis on heart infusion agar with 5% rabbit or human blood; no growth on MacConkey; ferments glucose (no gas), maltose and certain other carbohydrates, but not mannitol (serum added); indophenol oxidase and catalase not produced; starch and hippurate hydrolysed; resistant to sulphonamides, susceptible to 10μg metronidazole disc; normal flora of female genital tract (moderate numbers; 12-47% of vaginal samples), urinary tract; world-wide distribution; cause of amnionitis, chorioamnionitis, endometritis, bacteremia and septicemia (obstetric patients, rarely from prostate in males); assumed to be aetiologically significant in vaginosis (epithelial cells covered with masses of bacteria ('clue cells') seen in vaginal discharge), urethritis and acute cystitis; treatment: metronidazole, tinidazole, nimorazole, clindamycin, Acigel™; 100% susceptible to imipenem; resistant to ciprofloxacin

Subclass Coriobacteridae

Order Coriobacteriales

Suborder Coriobacterineae

Family Coriobacteriaceae

Atopobium parvulus: susceptible to metronidazole and novobiocin; resistant to SPS; lactic and acetic acids produced

A.rimae: new species; anaerobic

Eggerthella lenta: short coccoidal rods, diptheroidal; glucose not fermented; causes bacteraemia and septicemia; susceptible to meropenem (MIC 0.13 mg/L)

Olsenella uli: anaerobic

Phylum Bacteroidetes

Class Bacteroidia

Order Bacteroidales

Family Bacteroidaceae: never form spores; opportunistic pathogens causing wound and burn infections, septicemia, abscesses, other suppurative lesions; lack oxidative mechanism for active transport of aminoglycosides into cell; grow on blood media containing vitamin K and kanamycin

Anaerorhabdus furcosa: pleomorphic bifurcated cells; normal flora of gastrointestinal tract

Bacteroides: strictly anaerobic Gram negative rods and filaments; nonsporeforming; motile by peritrichous flagella or nonmotile; does not produce butyric acid or only lactic acid or acetic acid and H_2S; normal flora of mouth (large numbers), tonsils (usually present), colon (predominant organism), lower ileum (predominant organism), female external genitalia (usually present), vagina (usually present), urethra (usually present), cervix (usually present); anaerobic Gram negative bacilli most frequently isolated in pure culture (antibiotics in medium help in isolation); causes abdominal abscess (40% of isolates), abortional and puerperal infection, abscesses, balanoposthitis, 2-6% of bacteraemia and septicemia, cellulitis, cervical fascial space infections, cholecystitis, complications of surgical procedures (especially in females), cranial parameningeal deep fascial space infections, acute empyema, endocarditis, endometritis, enteritis, enterocolitis, ischiorectal abscess, local and generalised sepsis, lung abscess, lung gangrene, chronic mastitis and breast abscess, post-neonatal pyogenic meningitis (associated with surgery), urethritis, parametritis, pelvic abscess, pelvic inflammatory disease, peritonitis, tubo-ovarian abscess, vaginosis, chronic otitis externa; predisposing factors trauma or surgery, alcoholic liver disease, diabetes mellitus, malignancy (solid tumours), atherosclerosis, prematurity, end stage renal disease; KDO and heptose absent from lipopolysaccharide, very low toxicity; treatment: metronidazole, chloramphenicol, erythromycin, clindamycin; resistant to ciprofloxacin, ofloxacin, pefloxacin, lomefloxacin, enoxacin, cefuroxime, piperacillin, gentamicin

B.capillosus: normal flora of gastrointestinal tract, cervix, vagina, urethra; causes bone and soft tissue infection, female genital tract infection (3% of cases; acute salpingitis), intraabdominal abscess, lung abscess, peritonitis, postoperative wound infection (abdominal, head and neck), septicemia (8% of septicemia associated with infections of female genital tract), submandibular abscess; elaborates collagenase; susceptible to chloramphenicol, metronidazole, doxycycline

B.coagulans: normal flora of gastrointestinal tract, cervix, vagina; causes bone and soft tissue infection; susceptible to penicillin (MIC $\leq$ 0.062 mg/L), ampicillin ($\leq$ 0.062 mg/L)

B.eggerthii: *B.fragilis* group; normal flora of gastrointestinal tract; causes abdominal wound infection, intraabdominal abscess, peritonitis

B.fragilis: small Gram negative rod often showing irregular staining and moderate pleomorphism, encapsulated; grey, entire colonies; catalase positive, inhibited by 0.1% deoxycholate, not inhibited by 20% bile + 0.1% deoxycholate, bile-esculin positive, no butyric acid from glucose or amino acids, end pH glucose 5.0-5.4, no formic acid from threonine, resistant to penicillin G (zone of inhibition < 20 mm with 2U disc), relatively susceptible to erythromycin (17-45 mm zone with 60 μg disc), usually resistant to colistin (no zone with 10 μg disc), no zone with 1000 μg kanamycin disc, resistant to vancomycin (5μg disc), sensitive to rifampicin (15 μg disc), resistant to penicillin (2 U disc); normal flora of large intestine and female genital tract; anaerobe most frequently isolated from clinical material (77% of *Bacteroides* isolated from blood, 67% from urine, 51% from surgical wounds, 50% from respiratory tract, 37% from body fluids); causes 3% of surgical wound infections, female genital tract and pelvic infection (79%), infections in abnormal host (surgical procedure), intraabdominal abscess (54% of anaerobic infections), local and generalised sepsis, meningitis, pleuropulmonary infections (including pulmonary abscess), bacteremia and septicemia (70% of anaerobic, 50% of septicemia associated with infections of female genital tract), 68% of anaerobic perirectal abscess (including perianal and perirectal abscess and cellulitis in patients with malignant disease), 50% of anaerobic decubitus ulcers, 35% of anaerobic miscellaneous soft tissue infections below waist, 30% of anaerobic foot ulcers, 12% of anaerobic osteomyelitis and osteochondritis, acute diarrhoea and/or vomiting, acute cystitis, tubo-ovarian abscess, perinatal generalised disease, psoas abscess; extracellular; capsule inhibits phagocytic attachment and ingestion, promotes abscess formation, ? adhesin; elaborates collagenase, hyaluronidase, chondroitin sulphatase, fibrinolysin, neuraminidase, heparinase, DNAse, gelatinase, superoxide dismutase; susceptible to metronidazole/tinidazole (< 5% resistance), clindamycin, lincomycin, chloramphenicol, minocycline (MIC < 0.03 mg/L), imipenem, meropenem (0.5 mg/L), thienamycin (100%), amoxycillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, gatifloxacin, moxifloxacin; 100% intrinsic resistance (due to β-lactamase) to penicillin, amoxycillin, ampicillin, cephalosporins except cefoxitin and cefotetan

B.ovatus: *B.fragilis* group; mannitol fermented; normal flora of large intestine and female genital tract; 25% of *Bacteroides* isolates from respiratory tract, 11% from body fluids, 7% from surgical wounds, 5% from blood; causes infections in abnormal host; susceptible to imipenem (100% at 0.5 mg/L), meropenem (0.5 mg/L), metronidazole (100% at 1 mg/L); 99% resistant to penicillin, 22% resistant to clindamycin, 46% resistant to cefoxitin

B.stercoris: *B.fragilis* group

B.tectus: possibly related to *B.fragilis* group

B.thetaiotaomicron: *B.fragilis* group; normal flora of large intestine and female genital tract; 33% of *Bacteroides* isolates from urine, 25% from body fluids, 19% from surgical wounds, 15% from blood, 32% of anaerobes from perirectal abscess, 30% of anaerobes from intraabdominal infection, 26% of anaerobes from decubitus ulcers, 15% of anaerobes from miscellaneous soft tissue infections below waist; causes infections in abnormal host; susceptible to imipenem (100% at 0.5 mg/L), meropenem (0.5 mg/L); 100% resistant to penicillin, 16% resistant to clindamycin, 5% resistant to cefoxitin

B.uniformis: *B.fragilis* group; 8% of *Bacteroidees* isolates from body fluids, 6% from surgical wound, 1% from blood; susceptible to meropenem (0.5 mg/L); 98% resistant to penicillin, 20% resistant to clindamycin, 14% resistant to cefoxitin

B.vulgatus: *B.fragilis* group; normal flora of large intestine and female genital tract; 25% of *Bacteroides* isolates from respiratory tract, 9% from surgical wounds, 7% from body fluids; causes infections in abnormal host; susceptible to meropenem (0.5 mg/L), metronidazole (100% at 1 mg/L), 92% susceptible to cefoxitin; 92% resistant to penicillin, 18% resistant to clindamycin

Family Porphyromonadaceae

***Dysgonomonas capnocytophagoides*:** small coccoid to short rods; asporogenous; nonmotile; facultatively anaerobic; fastidious; no growth on MacConkey; indophenol oxidase and catalase not produced; ferments glucose (no gas), xylose, lactose, sucrose and maltose (with serum); usually produces indole weakly; hydrolyses esculin; nitrate not reduced; isolated from human blood, wound, urine, peritoneal fluid, umbilicus, abscess, abdominal tap, stool and genital tract; associated with chronic diarrhoea in patients with common variable hypogammaglobulinemia

Odoribacter splanchnicus: normal flora of gastrointestinal tract, vagina; causes abdominal wound infection, intraabdominal abscess, liver abscess, peritonitis; susceptible to penicillin, ampicillin, carbenicillin, cephazolin, cefoxitin, cefoperazone, chloramphenicol, clindamycin, erythromycin, metronidazole; resistant to cephalothin, cefaclor

Parabacteroides distasonis: normal flora of large intestine and female genital tract; causes infections in abnormal host; susceptible to clindamycin (100% at 0.03 mg/L), metronidazole (100% at 0.5 mg/L), imipenem (100% at 1 mg/L), meropenem (1 mg/L)

Porphyromonas asaccharolytica: brown or black pigment, brick-red fluorescence with UV light; α-fucosidase positive; normal flora of female genital tract and oral cavity; causes gingivitis and periodontitis, chronic otitis externa, severe erosive balanoposthitis, urethritis; 26% of anaerobes isolated from perirectal abscess, 17% of anaerobes isolated from decubitus ulcers, 10% of anaerobes isolated from foot ulcers, 10% of anaerobes isolated from miscellaneous soft tissue infections above the waist; susceptible to meropenem (MIC 0.06 mg/L)

P.endodontalis: does not produce α-fucosidase, trypsin-like enzyme or phenylacetic acid, does not agglutinate sheep erythrocytes

P.gingivalis: produces trypsin-like enzyme, phenylacetic acid, agglutinates sheep erythrocytes; dominant organism in rapidly progressive periodontitis; adheres to crevicular epithelium, Gram positive bacteria, red blood cells; capsule antiphagocytic; elaborates collagenase, IgA protease, IgG protease

Tannerella

Bacteroides forsythus: ? involved in periodontitis

Family Prevotellaceae

Prevotella bivia: normal flora of oropharynx, vagina; causes acute salpingitis, Bartholin cyst infection, breast abscess, infections in blood, bone and soft tissue, head and neck, lungs and pleural space, urogenital tract, pneumonia, postoperative wound infection, postpartum endometritis; elaborates neuraminidase; susceptible to clindamycin (MIC ≤ 0.25 mg/L), meropenem (0.5 mg/L), carbenicillin, cefamandole, cefoxitin, cefoperazone, moxalactam, chloramphenicol, erythromycin, metronidazole

P.buccae: normal flora of oropharynx, gastrointestinal tract; causes abdominal wound infections, brain abscess, cellulitis, empyema, infections of abdomen, blood, bone and soft tissue, central nervous system, head and neck, lungs and pleural space, intraabdominal abscess, lung abscess, peritonitis, pneumonia, postoperative wound infection, submandibular abscess; susceptible to cefoxitin, chloramphenicol, clindamycin, metronidazole

P.dentalis: new species

P.disiens: normal flora of oropharynx, vagina; causes acute salpingitis, breast abscess, infections of blood, bone and soft tissue, head and neck, lungs and pleural space, urogenital tract, perinatal generalised disease, pneumonia, postoperative wound infection; treatment: metronidazole; also susceptible to meropenem (MIC 0.25 mg/L), carbenicillin, clindamycin, erythromycin

P.intermedia: causes gingivitis and periodontitis, chronic otitis externa

P.melaninogenica: encapsulated, often coccobacillary; characteristically produces a black pigment on blood agar (may be nonpigmented or pigment very slowly), red fluorescence of young colonies on blood agar under UV light; inhibited by bile and 0.1% deoxycholate, fermentation patterns variable, ≥ 20 mm zone of inhibition with 2U penicillin disc, ≥ 15 mm zone of inhibition with 15 μg rifampicin disc, usually little or no zone with 1000 g kanamycin disc, 30-74 mm zone with 60 μg erythromycin disc, kanamycin resistant, colistin variable; normal flora of female genital tract and oral cavity; causes balanoposthtitis, female genital tract infection (24%), infections in abnormal host, non-specific urethritis, orodental infections (gingivitis and periodontitis; 11% of anaerobic infections), pleuropneumonia infections (including pulmonary abscess; in 23% of transtracheal aspirates and pleural fluid specimens growing anaerobes), septicemia (8% of septicemia associated with female genital tract infection), endocarditis (polymicrobial), 40% of anaerobic head and neck infections, 20% of anaerobic human bite infections; adheres to crevicular epithelium, Gram positive bacteria, vaginal epithelium; capsule antiphagocytic, inhibits macrophage migration, promotes abscess formation; elaborates collagenase, IgA protease, IgG protease, neuraminidase, DNAse, phospholipase A, hyaluronidase, fibrinolysin; susceptible to metronidazole, tinidazole, lincomycin, cephalexin, cephalothin, cephazolin, cefaclor, cefuroxime (0.1 mg/L), cefotaxime, ceftriaxone, cefepime, ceftazidime, cefotetan, cefoxitin, erythromycin (0.1 mg/L), clindamycin (0.1-0.25 mg/L), meropenem (0.5 mg/L), imipenem (99%), amoxycillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, azithromycin, clarithromycin, erythromycin, roxithromycin, chloramphenicol

P.nigrescens: new species

P.oralis: no red fluorescence of young colonies on blood agar under UV or brown or black pigment on blood agar, may have granular growth in broth; lack of growth in bile, inhibited by 0.1% deoxycholate, no butyric acid from glucose or amino acids, no propionic acid from threonine, mannitol fermented, no or slight gas from glucose; susceptible to penicillin (≥ 20 mm zone of inhibition with 2 U disc), ≥ 15 mm zone with 15 μg rifampicin disc, usually little or no zone with 1000 μg kanamycin, 37-70 mm zone with 60 μg erythromycin disc; normal flora of oropharynx; causes infections in abnormal host, orodental infections, necrotising pneumonia; elaborates collagenase, neuraminidase; susceptible to meropenem (MIC 0.25 mg/L)

P.ruminicola: normal flora of vagina and gastroinetestinal tract; elaborates DNAse; causes bone and soft tissue infection, pneumonia; susceptible to clindamycin (MIC ≤ 0.062 mg/L)

Family Rikenellaceae

Alistipes putredinis: inhibited by 0.1% deoxycholate, not inhibited by 20% bile + 0.1% deoxycholate, no butyric acid from glucose or amino acids, carbohydrates not fermented, no pitting of agar, gas from glucose, indole positive, most catalase positive; normal flora of gastrointestinal tract; causes acute salpingitis, bone and soft tissue infection, intraabdominal abscess, peritonitis; susceptible to cefoxitin, chloramphenicol, clindamycin, erythromycin, metronidazole

Class Flavobacteria
Order Flavobacteriales
Family Flavobacteriaceae

Capnocytophaga: Gram negative thin, filamentous rods with tapered ends; asporogenous; some strains motile with a single polar or lateral flagellum; gliding motility; frequently produces yellow to orange pigment; facultatively anaerobic; growth requires, or enhanced by, CO_2; fastidious; no growth on MacConkey; esculin hydrolysis variable; species difficult to distinguish; catalase usually negative, oxidase usually negative; indole negative; ferments glucose (no gas), maltose, sucrose, usually lactose, not mannitol or xylose; ONPG positive; natural habitat periodontal pockets of humans; isolated from human sputum, throat, blood, urine, vagina, pleural fluid and CSF; a rare opportunist; cause of mediastinal abscess in a competent host, sepsis in granulocytopenic patients, periodontal disease and septic arthritis in infants, acute sinusitis, acute empyema (rare), pulmonary abscess, amnionitis, chorioamnionitis (rare), local and generalised sepsis, peritonitis (primary and secondary), 0.1% of bacteraemia and septicemia (especially with oral mucositis), osteomyelitis and osteochondritis, purulent conjunctivitis; growth stimulated by excess iron; treatment: penicillin; also susceptible to ciprofloxacin (MIC 0.05-0.12 mg/L), ofloxacin (0.25-0.5 mg/L), pefloxacin (0.5 mg/L)

C.canimorsus: moderate to long thin rods, frequently slightly tapered, and with occasional spindle forms; asporogenous; nonmotile; facultatively anaerobic; fastidious; growth requires, or enhanced by, CO_2; indophenol oxidase and catalase produced; ferments glucose (no gas), lactose and maltose (with serum); positive test reactions for esculin and arginine dihydrolase; negative test reactions for growth on MacConkey, urease, nitrate and indole; natural habitat oral mucosa of animals, particularly dogs; an opportunist, infecting mostly patients with underlying diseases and patients with impaired host defence after splenectomy; associated with bites of, or exposure to, dogs; causes cellulitis, bacteraemia and septicemia, meningitis (in splenectomised or alcoholics following dog or cat bite), endocarditis; susceptible to penicillin (95%), amoxycillin-clavulanate, cefoxitin, erythromycin, tetracycline, clindamycin

C.cynodegmi: associated with septicemia or meningitis following dog bite

Chryseobacterium gleum: colonies viscous to mucoid and difficult to remove from surface of agar media; other phenotypic properties similar to *F.indologenes*; most strains isolated from human clinical specimens; vaginal specimens most common source; also recovered from abdominal tap, dialysis fluid, CSF, wound swab and peritoneal swab; clinical significance uncertain

C.indologenes: colonies produce an intracellular bright yellow pigment; oxidative in maltose and other carbohydrates, but usually not lactose or mannitol; proteolytic; indole produced; tests for ONPG and extracellular DNAse usually negative; esculin and starch hydrolysed; occasional strains reduce nitrate (no gas) and produce urease; natural habitat soil and water; frequently recovered from wet surfaces and water in hospital environment, as well as numerous clinical specimens, such as blood, sputum, throat, urine, lung, CSF, brain, nose and trachea; rarely clinically significant; associated with septicemia and meningitis in hospitalised patients

Elizabethkingia

F.meningosepticum: pale yellow or nonpigmented colonies on blood agar in 24 h; oxidase positive; indole produced; ONPG, esculin, DNA and gelatine hydrolysed; oxidative in maltose and other carbohydrates, including lactose and mannitol; nitrate not reduced; urease and amylase usually not produced; other phenotypic properties similar to *F.indologenes*; isolated from soil, water, hospital environment and human CSF, blood, urine, trachea, sputum, eye and nose; highly virulent for prematures; occasionally causes bacteremia and septicemia in leukemia, endocarditis in rheumatic heart disease, open heart surgery and i.v. drug abuse, endophthalmitis (postoperative), meningitis in neonates and adult immunocompromised, acute skin ulcers, burn infections, nosocomial infections; treatment: rifampicin, sulphadiazine, clindamycin, ciprofloxacin

Empedobacter brevis: colonies yellow with green edges; proteolytic; indole and DNAse produced; fails to hydrolyse ONPG, urea, esculin and starch; oxidises only a few carbohydrates (maltose and glucose); isolated from canal water and human clinical specimens, including urine, eye swab, bronchial secretion and blood; clinical significance unknown

Flavobacterium: simple rod, non-motile, asporogenous; obligately aerobic; some species produce brilliant yellow colonies; water-insoluble yellow or orange carotenoid pigment, very pale and not easily detectable in many species; pigment production variable on media that support growth; glutamate and undetermined vitamins required as organic growth factors; growth on MacConkey poor or negative; growth optimal at 30°C, no growth at 42°C; growth on SS usually negative; oxidative (delayed) or nonreactive; non-agar or cellulose digester; actively proteolytic, hydrolysing gelatine and casein; oxidase positive; catalase produced; indole formed by all but 1 species; some species weakly indole positive; lysine decarboxylase, arginine dihydrolase and ornithine decarboxylase negative; nitrate reduction and glucose variable; widely distributed in soil and water; also found in hospital environment and in human clinical material; normal flora of large intestine and lower ileum; causes bacteremia, meningitis, infections in abnormal host; susceptible to ciprofloxacin (MIC 0.5 mg/L); strains of most species resistant to penicillin and polymyxin

Myroides odoratus: colonies large, with a tendency to spread on agar surface, yellowish-green in colour; non-oxidative; urea, DNA and gelatine hydrolysed; nitrite reduced (variable) to gas, but not nitrate; ONPG, esculin and starch not hydrolysed; indole not produced; usually exhibits a fruity odour; isolated from environment and human clinical specimens,

especially urine, but also wound swab, ulcer, ear, blood and sputum; rarely clinically significant; associated with post-operative and post-traumatic foot infection and infant ventriculitis

CDC Group IIe: *Flavobacterium*-like phenotypic properties; indole produced; unlike other *Flavobacterium*, gelatinase not produced; ONPG, urea, esculin and DNA not hydrolysed; growth fails in O-F medium, test oxidative activity produced from glucose and maltose in a modified O-F base medium; isolated from human blood, urine and genital sites; cause of meningitis; susceptible to penicillin and polymyxin

CDC Group IIh: *Flavobacterium*-like phenotypic properties; indole produced; oxidative in a limited number of carbohydrates, usually maltose and xylose only; esculin, starch, gelatine and DNA hydrolysed; ONPG and urea not hydrolysed; susceptible to penicillin, but not polymyxin; isolated primarily from respiratory tract of animals; recovered from human CSF and ear as a saprophyte

CDC group IIi: *Flavobacterium*-like phenotypic properties; indole produced; unlike other *Flavobacterium*, gelatinase not produced; oxidative in a wide range of carbohydrates, but not mannitol; ONPG and esculin hydrolysed; urea and DNA not hydrolysed; indole production and lack of urease activity usually distinguish this species from phenotypically similar, but unrelated, *Sphingobacterium multivorum*; isolated as a saprophyte from human blood, urine and wound

Riemerella anatipestifer: rods, frequently pleomorphic; produces a brown, water-soluble pigment; aerobic; fastidious; oxidative in glucose and maltose (weakly); catalase and indophenol oxidase produced; positive test reactions for arginine dihydrolase, urease and gelatinase (late); negative test reactions for growth on MacConkey, nitrate and indole; agent of septicemia in ducks, geese and turkeys

Weeksella: rod-shaped; asporogenous; obligately aerobic; indophenol oxidase and catalase produced; nonmotile; indole formed; actively proteolytic; nitrate and nitrite not reduced; no acid produced from carbohydrates; yellow pigment usually not produced; susceptible to penicillin; apparently not isolated from general environment; commensal of humans and other warm-blooded animals

W.virosa: colonies very mucoid, moist, with a tendency to stick to the agar surface; usually grows at 42°C; urea not hydrolysed; growth occurs in O-F basal medium (alkaline reaction); susceptible to penicillin and polymyxin; strict parasite or saprophyte; recovered primarily from human urine, vaginal and cervical specimens; rarely clinically significant; cause of postsurgical septicemia; susceptible to clindamycin (MIC $\leq$ 0.03 mg/L)

W.zoohelcum: colonies butyrous, sticky and difficult to remove from agar surface; distinguished from *W.virosa* by rapid urea hydrolysis, failure to grow in O-F basal medium and at 42°C and susceptibility to penicillin but not polymyxin; strict parasite or saprophyte; recovered from oral cavity of dogs and cats; isolated from infected human wounds from dog and cat bites and scratches; cause of meningitis

Class Sphingobacteria

Order Sphingobacteriales

Family Flexibacteriaceae

Flectobacillus: oxidative, pale pink or rose pigment, highly curved rod, oxidase positive

Family Sphingobacteriaceae

Sphingobacterium: small straight rods; nonmotile; asporogenous; nonflagellated, but exhibit gliding movement on agar surface; pale to bright yellow pigment produced by most species; obligately aerobic; indophenol oxidase and catalase produced; oxidative in glucose and a wide range of other carbohydrates; ONPG, urea and esculin hydrolysed; failure to produce indole and, usually, gelatinase distinguishes this genus from *Flavobacterium*; primarily isolated from human clinical materials

S.mizutaii: oxidative activity from rhamnose; urea hydrolysis and nitrite reduction to gas strain variable; otherwise similar to *S.multivorum*; isolated from human ventricular fluid, synovial fluid and urine; cause of meningitis in prematures

S.multivorum: rhamnose and mannitol not oxidised; nitrate and nitrite not reduced; no growth at 42°C; otherwise similar to other species of this genus; isolated from soil, turnip and various clinical specimens, such as lung, eye, semen, throat, peritoneal fluid, blood, abdominal fluid, urine, skin, serous cavity fluid, CSF, spleen, wound and eye discharge; rarely clinically significant; associated with spontaneous peritonitis, septicemia in a haemodialysed patient and septicemia in a patient with lymphoma; susceptible to minocycline (MIC 0.5-1 mg/L)

S.spiritovorum: oxidises rhamnose and mannitol; otherwise similar to *S.multivorum*; isolated from human blood, wound swab, peritoneal fluid, urine, sputum, bone marrow, vaginal swab and intrauterine specimen, as well as from sink tap and humidifier sponge; clinical significance not known

S.thalpophilum: reduces nitrate (no gas) and grows at 42°C; otherwise similar to *S.multivorum*; isolated from human clinical sources, including blood, abscess and wound swab; clinical significance not known

Phylum Chlamydiae

Class Chlamydiae

Order Chlamydiales: small cellular forms, possibly degenerate Gram negatives, highly evolved to an intracellular parasitic life mode with concurrent loss of certain important energy-yielding metabolic functions; no growth outside host cell;

independent protein synthesis; variable rigid cell enveloped; susceptible to antibiotics; reproduction by fission; DNA and RNA; cell wall or cell wall peptidoglycan present; do not require sterols

Family Chlamydiaceae

Chlamydia: no growth in nonliving media; Gram negative with cell wall similar to other Gram negative bacteria; possesses both RNA and DNA; reproduces by binary fission; possesses ribosomes; susceptible to antibiotics; elementary body ($\approx 0.3\mu m$) rigid cell wall, relatively resistant to sonication, resistant to trypsin, subunit in cell envelope, RNA:DNA content = 1:1, toxic for mice, isolated organisms infectious, adapted for extracellular survival; reticulate body (0.5-1 μm) fragile cell wall, sensitive to sonication, lysed by trypsin, no subunit in envelope, RNA:DNA = 3:1, nontoxic for mice, isolated organisms not infectious, adapted for intracellular growth; causes reactive arthritis, bartholinitis, purulent cervicitis, conjunctivitis, acute dacrocystitis, adenitis and canaliculitis, encephalitis, hepatic granuloma, pneumonia, 35-50% of non-gonococcal urethritis, ? sweating disease; $\approx$ 7000 total notified cases/y in Australia; attaches to conjunctival or urethral epithelium (? sialic acid-containing receptors on epithelial cell); infection generally confined to epithelial surface of conjunctiva (trachoma, inclusion conjunctivitis) or urogenital tract (TRIC agents in nonspecific urethritis); growth stimulated by excess iron; susceptible to gatifloxacin, moxifloxacin, tetracycline, doxycycline, minocycline, azithromycin, clarithromycin, erythromycin, roxithromycin; resistant to ciprofloxacin

C.psittaci: not inhibited by neuraminidase, not pathogenic for monkeys or mouse brains, resistant to sulphonamides, more diffuse inclusion, no glycogen in inclusion, G+C $\approx$ 41%; principal hosts birds and mammals; causes ornithosis (psittacosis), splotchy rash with pulmonary involvement, many clinical and subclinical diseases of mammals and birds; enters across epithelial surface of respiratory tract and subsequently spreads through body; inhibits lysosome-phagosome fusion; persists in lung (rarely in man; ? infectious, not shed to exterior) and spleen of bird (may be infectious, shed to exterior, activation occurs); penicillin inhibits conversion of reticulate bodies to elementary bodies; diagnosis: complement fixation test (*C.trachomatis* antigen); treatment: doxycycline, erythromycin, tetracycline, rifampicin

C.trachomatis: more compact inclusion, glycogen present in inclusion, G+C $\approx$ 44%, susceptible to sulphonamides; principal host humans; serotypes A-K (trachoma, inclusion conjunctivitis, urethritis, etc) inhibited by neuraminidase; serotype L (LGV) not inhibited by neuraminidase, pathogenic for mouse brains; causes chlamydial lymphogranuloma (LGV biovar), dysuria-frequency (urethral) syndrome, mucopurulent cervicitis, endometritis, acute epididymitis and epididyomoorchitis (mainly heterosexual men), orchitis, parametritis, pelvic abscess, pelvic inflammatory disease, perihepatitis, peritonitis, primary pneumonia in infants and in AIDS, proctitis, salpingitis, trachoma, 35-50% of nongonococcal urethritis, vaginitis; increased infectiousness in abnormal host; LGV strain enters across epithelial surface of urogenital tract and subsequently spreads through body; TRIC strain persists in conjunctiva (infectious, ? shed to exterior), causing chronic disease and blindness; 500 genes; diagnosis: culture, PCR, direct immunofluorescence, enzyme immunoassay, DNA probe; treatment: tetracycline (MIC 0.5 mg/L), erythromycin (0.5 mg/L), doxycycline, sulphamethoxazole, sulphisoxazole, chlortetracycline, oxytetracycline, sulphadiazine

Chlamydophila pneumoniae: causes bronchitis, nonexudative pharyngitis and tonsillitis, pneumonia, acute sinusitis, endocarditis, ? chronic asthma, ? atherosclerosis, ? multiple sclerosis; growth strongly suppressed by iron restriction; detection: isolation, microimmunofluorescent antibody; treatment: tetracycline

Phylum Cyanobacteria: 'blue-green algae'

Order Chroococcales

Microcystis : 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (microcystin)

Oreder Nostocales

Family Nostocaceae

Anabaena: 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (microcystin) and neurotoxicity (anatoxin and saxitoxin)

Aphanizomenon: 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (cylindrospermopsin) and neurotoxicity (anatoxin and saxitoxin)

Cylindrospermospsis: 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (cylindrospermopsin) and neurotoxicity (saxitoxin)

Nodularia: 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (nodularin)

Nostoc: 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (microcystin)

Order Oscillatoriales

Lyngbya: 'indigenous' in freshwater; forms blooms; causes neurotoxicity (anatoxin)

Oscillatoria: 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (microcystin) and neurotoxicity (anatoxin)

Order Stigonematales

Umezakia: 'indigenous' in freshwater; forms blooms; causes hepatotoxicity (cylindrospermopsin)

Phylum Firmicutes: intracellular osmotic pressure of Gram positive bacteria is 2 or more times that of Gram negatives

Class Bacilli
Order Bacillales
Family Bacillaceae

Bacillus: large, sporeforming bacillus, Gram positive but some species readily decolourised; heat-resistant endospores associated with uptake of calcium ions and synthesis of dipicolinic acid; germination requires injury to spore coat, water, L-alanine and replenishment of nitrogen and carbon; aerobic ± anaerobic growth; catalase positive; normal flora of large intestine, skin; frequent laboratory contaminant; causes bacteraemia and septicemia in compromised patients, food poisoning, iridocyclitis, meningitis (infrequent in compromised patients, very rare in neonates), panophthalmitis, wound infection; growth stimulated by excess iron; treatment: vancomycin (< 5% resistance in Australia), clindamycin; also susceptible to irloxacin (MIC 0.06 mg/L), ciprofloxacin (0.2-1 mg/L), norfloxacin (1mg/L), enoxacin (1 mg/L), gentamicin

B.anthracis: large (1-1.5 x 3-5 µm), Gram positive, square-ended bacillus with oval, central to subterminal, non-swelling spore (1 x 1.5 µm); single or in chains of 2-4 and encapsulated in clinical specimens but non-encapsulated and long chains from sheep blood agar; nonmotile; penicillin susceptible, producing spherical cells in vicinity of disc; colonies on sheep blood agar grey-white to white, generally smaller than *B.cereus,* nonhaemolytic, flat or slightly convex, irregularly round, with slightly undulate edges and ground glass appearance, often many comma-shaped outgrowths 'Medusa head' colony), tenacious consistency, standing up like egg white when teased with a loop; colonies on nutrient agar + 0.8% bicarbonate in 5% CO_2 raised and mucoid (virulent strains) and yield heavily encapsulated cells; no growth on MacConkey agar; litmus milk not peptonised, salicin negative, VP positive, gelatine liquefaction negative or slow, lecithinase weakly positive; lysed by γ phage; elaborates anthrax toxin; possesses plasmids pX01 and pX02; virulent in mice and guinea pig; M'Fadzean reaction in killed mice; fluorescent antibody to *B.anthracis* positive; causes anthrax (≈ 5 cases (no deaths)/y in USA), bacteraemia and septicemia, haemorrhagic meningitis; pathogen of herbivorous animals, who ingest spores; occasional human infection; systemic disease following local lesion at inoculation site; inhibits phagocytic attachment and ingestion; toxic complex kills phagocytes; cell wall poly-D-glutamic acid resists killing by phagocytes and is associated with invasiveness; carried in blood free in plasma; 3 factors form a toxic complex and cause increased vascular permeability, causing oedema and haemorrhage (primary lesion), circulatory failure (systemic disease); characteristic appearance in chest X-ray of inhalation anthrax results from lymphadenopathy and mediastinal hemorrhage; antibodies to capsular material not protective; antibodies to toxin, or possibly to spontaneously 'toxoided' derivatives, confer specific immunity; resistance can be induced by immunisation with whole toxin or spores; treatment: penicillin, streptomycin, tetracycline, erythromycin, vancomycin

B.cereus: ubiquitous organism; diameter of vegetative cells ≥ 0.9 µm; motile; usually β-haemolytic on sheep blood agar, colonies slight green tinge, few or no comma-shaped outgrowths from colonies on blood agar; colonies on 0.7% bicarbonate agar in air or CO_2 rough, dull, grey, flat; anaerobic growth; litmus milk not peptonised; VP, catalase, lecithinase, nitrate, 6.5% NaCl, gelatine and lecithinase (strongly) positive; penicillin resistant; fluorescent antibody to *B.anthracis* negative; not lysed by γ phage; nonpathogenic to mouse and guinea pig; causes endocarditis (infrequent in valvular heart disease, i.v. drug abuse), endophthalmitis (posttraumatic, bloodborne) gastroenteritis (emetic type due to preformed heat-resistant enterotoxin, incubation period 1-6 h, vomiting median 9 h, almost invariably associated with ingestion of contaminated fried or reheated rice dishes; diarrhoeal type caused by heat-labile enterotoxin, more common, incubation period 6-24 h, abdominal cramps and watery diarrhoea median 20 h, most commonly associated with meats and sauces), local and generalised sepsis (prime cause of traumatic wound infections in tropics), panopthalmitis in drug abusers, infections in abnormal host, bacteraemia and meningitis in immunocompromised; treatment: vancomycin + carbapenem; flucloxacillin, clindamycin; also susceptible to ciprofloxacin (MIC 0.125 mg/L), enoxacin (1 mg/L); resistant to ceftazidime

B.megaterium: diameter of vegetative cells ≥ 0.9 µm; motile; no haemolysis on sheep blood agar; no growth on 10 mg/L penicillin agar, no growth on 0.7% bicarbonate agar in air, colonies in CO_2 smooth, dull yellow, raised; salicin and VP negative; peptonisation of litmus milk variable; causes infections in abnormal host

B.mycoides: spreading rhizoid colonies with marked tailing

B.subtilis: diameter of vegetative cells < 0.9 µm; grows at pH 6; VP, gelatine and starch positive; nitrate reduced to nitrite; common laboratory contaminant; causes conjunctivitis, infections in abnormal host

B.thuringiensis: crystalline parasporal inclusion; colonies slight green tinge

Bacillales Family XI Incertae Sedis

Gemella: no growth at 45°C or 10°C; catalase and bile esculin negative; no gas from glucose; may, on rare occasions, cause diseases of respiratory tract but no proof of causal role; susceptible to vancomycin

G.morbillorum: microaerophilic; susceptible to novobiocin; resistant to metronidazole and SPS; produces lactic and acetic acids; causes 13% of bacteremia and septicemia due to *'S.viridans'*

Family Listeriaceae

Listeria: small Gram positive rods and filaments, no spores; motile at 25°C, motile or nonmotile at 35°C; catalase, VP and esculinase positive; PYR and oxidase negative; bacitracin resistant; normal flora of upper respiratory tract; carried in blood associated with mononuclear cells; causes systemic infections in cell-mediated immunity disorders; growth stimulated by

excess iron; susceptible to penicillin, amoxy/ampicillin, piperacillin, piperacillin-tazobactam, meropenem, chloramphenicol, trimethoprim, cotrimoxazole, vancomycin, teicoplanin; synergy with aminoglycosides and cell wall active agent

L.grayi: nitrate positive

L.innocua: nonhemolytic, CAMP test negative

L.monocytogenes: motile; β-hemolytic; catalase, glucose, maltose, sucrose, salicin and CAMP test positive; H_2S not produced in triple sugar iron agar, nitrate negative; starch variable; found in sewage, soil, faeces of healthy animals and man, widespread in foods of virtually all types, normal flora of upper respiratory tract; causes listeriosis (highest mortality in neonatal infection; in most cases, origin unknown), premature or nonviable termination of pregnancy, localised external or internal abscesses, localised skin lesions (rare), amnnionitis, 0.2% of bacteremia and septicemia (low grade in gravida → influenza-like condition, case-fatality rate in perinatal period and in adults 11%), brain abscess (especially in leukemia and renal transplant recipients; case-fatality rate 57%), cervical adenitis, cholangitis and cholecystitis, endocarditis (in rheumatic fever, prosthetic heart valve, malignancy, immunosuppressed, following coronary artery bypass surgery; case-fatality rate 29%), endophthalmitis (oculoglandular listeriosis; uncommon), gastroenteritis, genital tract infection, prenatal and perinatal generalised disease, hepatitis (adult, neonatal and prenatal), hepatic abscess in diabetes, hepatic granuloma, infectious mononucleosis-like syndrome, keratoconjunctivitis, lymph gland infection, neonatal and postneonatal pyogenic and nonpyogenic meningitis and meningoencephalitis (2-3% of bacterial meningitis; incidence 0.04/100 000; case-fatality rate 30%; ≈ 50% nosocomial; 55% adult infections; most common in impaired cell-mediated immunity, neonates, immunosuppressed patients and those with underlying chronic disease), non-meningitic central nervous system infection (including rhombencephalitis in nonimmunosuppressed adults; mortality rate 42%), mycotic aneurism, myocarditis and pericarditis (cardiac transplantation and others), osteomyelitis and osteochondritis, peritonitis, pneumonia, purulent conjunctivitis, splenic abscess, stillbirth, vascular graft infection, infections in abnormal host (T-lymphocyte dysfunction); 56% of isolates from blood, 8% from CSF, 16% from blood and CSF; resists phagocytic oxidative attack; multiplies in macrophages; immunity cell-mediated (delayed type hypersensitivity activated macrophage +++); susceptible to interferon-γ, interferon-β, interferon-α, interleukin-4, interleukin-6, interleukin-1 and macrophage colony stimulatory factor-activated macrophages; interleukin-2, interleukin-6, granulocyte macrophage colony stimulatory factor, granulocyte stimulatory factor and tissue necrosis factor also induce autoimmune activity; diagnosis: indirect hemagglutination (4-fold rise in titre indicates active infection), enrichment in broths based on trypticase ± peptones + acriflavine dyes + nalidixic acid as selective agents (± potassium thiocyanate, cycloheximide), culture on blood agar + cycloheximide, colistin, cefotetan, fosfomycin and acriflavine; treatment: ampicillin (resistance not yet confirmed in Australia), amoxycillin (100% susceptible at 0.25 mg/L) or penicillin (0.25 mg/L) ± gentamicin (1 mg/L), i.v. cotrimoxazole (0.025 mg/L) followed by oral trimethoprim (0.12 mg/L), chloramphenicol or erythromycin (0.25 mg/L); also susceptible to rifampicin (0.06 mg/L), imipenem (0.06-0.125 mg/L), tetracycline (0.5 mg/L), vancomycin (1m/L); resistant to all cephalosporins, enoxacin, pefloxacin

Family Planococcaceae

Kurthia bessonii: motile at 35°C and 25°C; catalase positive, no reaction in O-F medium; normal habitat water; human infections unknown or extremely rare

Lysinibacillus

Bacillus sphaericus: spores spherical

Family Staphylococcaceae

Macrococcus caseolyticus: novobiocin susceptible; found in animals and animal products

Staphylococcus: Gram positive cocci, cells round, single and in groups, especially tetrads and botryoidal clusters; may be capsulated; cell wall teichoic acid, pentaglycine bridge in peptidoglycan; anaerobic growth in glucose, growth in 6.5% NaCl; may be β-haemolytic; nonadherent, large colonies; no growth on furoxone-Tween 80-red O agar; catalase positive, glucose fermented, bile esculin negative; aerobic acid production from glycerol in presence of erythromycin; usually resistant to 0.04 U bacitracin, resistant to lysozyme, usually susceptible to lysostaphin; DNA base composition 30-40% G+C; among most ubiquitous of bacteria; normal flora of skin, vagina (62%); frequently causes pyogenic and suppurative conditions, including appendicitis, boils, cholangitis and cholecystitis, discitis, endocarditis, post-neonatal pyogenic meningitis, perinephric abscess, postnatal infection, pulmonary abscess, septic arthritis, septicemia (including haemorrhagic fever), septicemia adrenal haemorrhage syndrome, thyroiditis, water-related infections; commonest skin invader; infection usually confined to epithelial surface of skin; extracellular; growth stimulated by excess iron; leucocidins (deoxyribonuclease, diphosphopyridine nucleotidase, nicotinamide adenine dinucleotidase) induce lysosomal discharge into cell cytoplasm killing phagocyte (both neutrophils and macrophages disrupted), protein A blocks Fc portion of antibody inhibiting opsonised phagocytosis, polysaccharide capsule in some strains, cell wall mucopeptide resists killing by phagocytes, ? catalase resists killing, hyaluronidase causes spread of infection; also produces large amounts of exotoxin, which may cause intoxication; primary bodily defence mechanism leucocyte bactericidal function; recovery from primary infection due to antibody; mean doubling time 20 minutes in vitro; treatment: cloxacillin, flucloxacillin, gentamicin, vancomycin, rifampicin, amoxycillin-clavulanate, cephalothin, sodium fusidate, clindamycin; also susceptible to irloxacin (MIC 0.5 mg/L), cephalexin, penicillin (β-lactamase negative), ampicillin (β-lactamase negative), methicillin; resistant to cefixime

S.arlettae: found in animals and animal products; novobiocin resistant

S.aureus: ribitol-N-acetylglucosamine cell wall teichoic acid; Gram positive cocci in clusters; colonies may be golden; anaerobic growth; catalase positive; glucose fermented, mannitol fermented, phosphatase, heat-resistant endonucleases, Staphyslide and tube coagulase positive (clumping factor reacts with fibrinogen, protein A reacts with Fc portion of human IgG; small colony variant methicillin resistant strains lack clumping factor); novobiocin susceptible; normal flora of skin, mouth, nasopharynx, tonsils, nose (adherence to nasal mucosa ++), large intestine, lower ileum, external genitalia (adherence to labium majus ++), anterior urethra (rare), vagina, cervix (3-17%), ear, eye (rare); phage typing identifies virulent strains; causes abortional and puerperal infections, abscesses, appendicitis, septic arthritis, 10-30% of bacteraemia and septicemia, balanitis, blepharitis, boils, 60% of brain and epidural abscess (common after trauma or surgery), acute bronchitis, burn infections, bursitis, carbuncles, 1% of carpal tunnel syndrome (+ 3% due to toxic shock syndrome), cat and dog bite infections, cellulitis, cerebrospinal fluid shunt infections, cervical fascial deep space infections, cholangitis and cholecystitis, chondritis, complication of pseudomembranous enterocolitis, compound fractures infections, purulent conjunctivitis, cranial parameningeal deep fascial space infections (immunocompromised and others), croup, acute cystitis, acute empyema, 10-32% of endocarditis (45% of *S.aureus* infections in drug addicts), endophthalmitis (postoperative, posttraumatic, septicemia), enteritis, enterotoxemia (food poisoning; organisms spread from nose, hands or septic lesion of food handler, multiply in poultry, pork, ham, beef, meat pies, sausages, custard, trifle, etc), post-antibiotic diarrhoea and enterocolitis (profuse watery diarrhoea, with dehydration, resulting from production of enterotoxins by antibiotic-resistant strains in gut lumen following administration of antibiotics), acute epididymitis and epididymoorchitis, 83% of false aneurism, folliculitis, furunculosis, adult hepatitis (in toxic shock syndrome), hepatic abscess, hiradenitis, hordeolum, human bite and clenched fist infections, impetigo and bullous impetigo, ischiorectal abscess, keratitis and iritis, laryngotracheitis, local and generalised sepsis, 3% of lymph gland infection, acute mastitis and breast abscess, mastoiditis, meningitis (0.5% of neonatal (late), 1-9% of postneonatal pyogenic), mycotic aneurism (3% of *S.aureus* infections in heroin addicts), nasal septal abscess, 1% of necrotising fasciitis, 55% of osteomyelitis and osteochondritis (+ 22% in combination with anaerobes), 16% of otitis externa (including rare malignant), otitis media, pancreatic abscess, paronychia, parotitis and submandibular sialadenitis, myocarditis and pericarditis (in granulocytopenia), perichondritis, perinatal generalised disease, peritonitis (primary and continuous ambulatory peritoneal dialysis), primary and secondary pneumonia (including diffuse interstitial, chronic pulmonary infection in cystic fibrosis), pulmonary abscess, postseptal cellulitis, prostatic abscess (younger patients), psoas abscess, pustulosis, acute pyelonephritis, pyoderma, erythematous rash ('staphylococcal scalding'), rhabdomyolysis, 12% of septic thrombophlebitis (associated with local trauma; 7% of *S.aureus* infections in heroin addicts), acute and chronic sinusitis, localised skin lesions, splenic abscess, stye, 15% of surgical wound infections (summer peak), sycosis barbae, symbiotic gangrene, thyroiditis, toxic epidermal neurolysis, toxic shock syndrome, acute tracheitis, chronic ulcers, urethritis, vaginitis in prepubertal girls and elderly women, 10% of nosocomial infection, infections in abnormal host (interrupted integument, surgical procedure, neutrophil dysfunction), systemic infections in chemotactic defect, C1, 2, 3, 4, factor B deficiency, granulocytopenia, microbicidal abnormality; α-toxin is cytotoxic and acts on cell membranes, causing necrosis at site of infection and systemic toxicity; leucocidin kills phagocytes (virulence factor); enterotoxin absorbed from intestine acts on vomiting centre in brain, causing nausea, vomiting, diarrhoea (food poisoning; incubation period 0.5-6 h); haemolysins and exfoliatin other toxins produced; inhibits phagocytic attachment and ingestion; cell wall N-acetylglucosamine linked to polyribitol phosphate (mucopeptide) associated with invasiveness (virulence factor); coagulase provides protection by fibrin deposition (virulence factor); fibronectin binding important in endocarditis; catalase, lipase, lysozyme, lactic acid dehydrogenase, acid phosphatase, protease, hyaluronidase, fibrinolysin, deoxyribonuclease, penicillinase other enzymes produced; teichoic acid and protein A significant factors; major host defence mechanisms β-lysin (+), phagocytes (+++), immune adherence (phagocytosis) (+); ultrastructure in vivo comparable to that if grown on a solid support medium and different from that if grown in a liquid medium; diagnosis: counterimmunoelectrophoresis (teichoic acid antibody $\geq$ 1:4; pleural fluid, sensitivity 86%), culture; methicillin resistance ranges from 2% in Switzerland to 74% in Hong Kong; non-MRSA susceptible to di/flucloxacillin, amoxycillin-clavulanate, piperacillin-tazobactam, ticarcillin-clavulanate, cephalexin, cefuroxime, cefotetan, cefoxitin, cephalothin (MIC 0.06-0.5 mg/L), cephazolin, cefaclor, cefpirome (0.5-1mg/L), cefepime, ceftazidime, thienamycin ($\leq$ 0.06 mg/L), mupirocin (0.06-0.12 mg/L), amikacin, gentamicin, tobramycin (0.25 mg/L), imipenem, meropenem (0.25 mg/L), teicoplanin (0.25-1 mg/L), gatifloxacin, moxifloxacin, doxycycline, tetracycline, minocycline, chloramphenicol, clindamycin, lincomycin, sodium fusidate, linezolid, synercid, rifampicin/rifabutin, vancomycin/teicoplanin, neomycin, bacitracin, resistant to cefixime, nalidixic acid, pipemidic acid; methicillin resistant 100% resistant to all penicillins, all cephalosporins, susceptible to vancomycin/teicoplanin (resistance not yet confirmed in Australia), linezolid, synercid, usually susceptible to novobiocin; 4-72% of community associated and 5-50% healthcare associated MRSA suspectible to erythromycin, 56-100% and 37-88% to clindamycin, 56-98% and 8-75% to fluoroquinolones, 73-99% and 58-94% to gentamicin, 86-100% and 88-92% to tetracycline, 84-100% and 82-100% to cotrimoxazole; in Australia, 85% of methicillin susceptible strains resistant (acquired resistance due to β-lactamase) to penicillin, amoxycillin, ampicillin, ticarcillin, piperacillin and azlocillin, 34% of all strains (13% of methicillin susceptible) resistant to erythromycin and other macrolides, 25% of all strains resistant to methicillin, dicloxacillin, cloxacillin, oxacillin, flucloxacillin and cephalosporins (significant geographic variation), 26% of all strains (3% of methicillin susceptible) resistant

to cotrimoxazole, 23% of all strains (5% of methicillin susceptible) resistant to tetracycline, 12% of MRSA resistant to rifampicin, 4% of MRSA resistant to fusidic acid, 12% of all strains (60% of MRSA) resistant to ciprofloxacin, 27% of all strains resistant to trimethoprim

S.auricularis: novobiocin susceptible; pathogenicity rare/undetermined

S.capitis: novobiocin susceptible, maltose negative; 1-44% of coagulase negative staphylococcal colonisers; uncommon pathogen; susceptible to meropenem (MIC 0.25 mg/L)

S.cohnii: novobiocin resistant; sucrose and xylose negative; no colonisers, 2% of coagulase negative staphylococcal disease isolates; susceptible to meropenem (MIC 1 mg/L)

S.epidermidis: glucose cell wall teichoic acid; yellow pigmented strains; anaerobic growth; glucose, maltose and phosphatase positive; mannitol, trehalose, glycerol and heat-resistant endonucleases negative; novobiocin susceptible; 57% of coagulase negative staphylococcal colonisers, 45-66% of disease isolates; normal flora of mouth, nose (adherence to nasal mucosa ++), tonsils, throat, external genitalia, anterior urethra (rare), vagina (57%); causes acne, pimples, catheter-induced bacteraemia in neutropenics (74% of bacteraemia and septicemia due to coagulase negative staphylococci), blepharitis, 2% of brain abscess, cerebrospinal fluid shunt infections, complication of cardiac surgery, acute cystitis, endocarditis, endometritis, catheter-induced septic arthritis in neutropenics, 5% of surgical wound infections, thrombophlebitis, 3% of noscomial infection, 12% of vascular graft infection, infections in abnormal host (interrupted integument); slime production important in endocarditis; susceptible to sodium fusidate, linezolid, synercid, vancomycin (MIC 0.5-1 mg/L; resistance reported from Slovak Republic), rifampicin; variably susceptible to di/flucloxacillin, amoxycillin-clavulanate, piperacillin-tazobactam, ticarcillin-clavulanate, imipenem, meropenem, clindamycin, lincomycin

S.equorum: novobiocin resistant; found in animals and animal products

S.felis: novobiocin susceptible; found in animals and animal products

S.gallinarum: novobiocin resistant; found in animals and animal products

S.haemolyticus: novobiocin susceptible; maltose and mannitol positive; 8% of coagulase negative staphylococcal colonisers, 10-38% of disease isolates; susceptible to ofloxacin (MIC 0.5 mg/L), pefloxacin (0.5 mg/L), ciprofloxacin (0.5-1 mg/L), enoxacin (1mg/L), amifloxacin (1mg/L)

S.hominis: novobiocin susceptible; maltose and trehalose positive; mannitol negative; 35% of coagulase negative staphylococcal colonisers, 4-15% of disease isolates, 14% of isolates from bacteraemia and septicemia; susceptible to ofloxacin (MIC 0.5 mg/L), ciprofloxacin (1 mg/L), amifloxacin (1mg/L), pefloxacin (1 mg/L)

S.hyicus: coagulase variable, novobiocin susceptible; found in animals and animal products

S.intermedius: 27% coagulase positive; causes dog bite wound infections; 100% susceptible to dicloxacillin, amoxycillin-clavulanate

S.kloosii: novobiocin resistant; found in animals and animal products

S.lentus: found predominantly in animal products

S.lugdunensis: tube coagulase negative, clumping factor usually positive, usually weak positive thermostable DNAse reaction; novobiocin susceptible, nitrofurantoin susceptible; urease, ornithine decarboxylase, PYR, glucose, fructose, sucrose, maltose, lactose, trehalose, N-acetylglucosamine positive; arginine dihydrolase, β-glactosidase, β-glucosidase, esculin, mannitol and raffinose negative; causes endocarditis (mainly community acquired, usually preexisting cardiac abnormality), venous catheter infection, peritonitis, endophthalmitis, wound infection, septic arthritis; susceptible to cotrimoxazole (MIC ≤ 0.03-0.06 mg/L), gentamicin (≤ 0.06 mg/L), tobramycin (≤ 0.06 mg/L), erythromycin (≤ 0.06 mg/L), pristinamycin (≤ 0.06 mg/L), minocycline (≤ 0.06 mg/L), fusidic acid (≤ 0.06 mg/L), rifampicin (≤ 0.06 mg/L), penicillin (≤ 0.06-1 mg/L), lincomycin (0.25 mg/L), teicoplanin (0.25-0.5 mg/L), kanamycin (0.25-0.5 mg/L), oxacillin (0.25-1 mg/L), pefloxacin (0.5 mg/L), meropenem (0.5 mg/L), vancomycin (0.5-1 mg/L)

S.saccharolyticus: resistant to novobiocin and SPS; susceptibility to metronidazole variable; produces formic and acetic acids

S.saprophyticus: ribitol-N-acetylglucosamine and glycerol-N-diacetylglucosamine cell wall teichoic acids; weak anaerobic growth; coagulase and Staphyslide negative (typically, reaction in both test and control); novobiocin resistant; weak glucose and sucrose fermentation; xylose, phosphatase and heat-resistant endonucleases negative; 2% of coagulase negative staphylococcal colonisers, 2-4% of disease isolates; causes chronic bacteriuria related to infected bladder or renal stones, acute cystitis and pyelonephritis in otherwise healthy young women, bacteraemia and septicemia (rare cases associated with sexual intercourse and/or urinary obstruction), endocarditis, prostatitis and vesiculitis, infections in abnormal host; susceptible to nitrofurantoin (100%), all penicillins, all cephalosporins, imipenem, meropenem (MIC 0.5 mg/L), chloramphenicol, clindamycin, lincomycin, macrolides, tetracyclines, linezolid, synercid, cotrimoxazole (5% resistance in USA), trimethoprim, vancomycin, teicoplanin, rifampicin/rifabutin, sodium fusidate

S.schleiferi subsp coagulans: coagulase positive; novobiocin susceptible; maltose and sucrose negative; uncommon pathogen in dog bite wounds

S.sciuri: 2% of coagulase negative staphylococcal colonisers, no disease isolates

S.simulans: novobiocin susceptible; maltose negative; uncommon pathogen

S.warneri: novobiocin susceptible; maltose and mannitol positive; occasional colonisers, 3% of coagulase negative staphylococci disease isolates, 6% of coagulase negative staphylococci isolated from bacteraemia and septicemia

S.xylosus: novobiocin resistant; xylose positive; sucrose negative; no colonisers, 2% of coagulase negative staphylococcal disease isolates

'Coagulase Negative Staphylococci': Gram positive cocci in clusters; catalase positive; coagulase negative; cause 5% of bacteraemia and septicemia, blepharitis, bursitis, cat and dog bite infections, 0.5% of carpal tunnel syndrome, endophthalmitis (postoperative, posttraumatic), generalised infections in patients in whom inanimate objects have been inserted into vascular system (valve prostheses, ventricular shunt devices, intravenous cannulae), human bite and clenched fist injury infections, local abscesses related to foreign bodies in tissues (joint prostheses), chronic mastitis and breast abscess, 1% of necrotising fasciitis, osteomyelitis and osteochondritis, 7% of otitis externa (including rare malignant), peritonitis (primary and associated with continuous peritoneal dialysis), pyelonephritis only after instrumentation (except *S.saprophyticus*), systemic infections in granulocytopenics; usually susceptible to vancomycin (< 5% resistance in Australia), rifampicin, fucidin; commonly susceptible to penicillin, methicillin, oxacillin, erythromycin, cotrimoxazole, trimethoprim

Order Lactobacillales

Family Aerococcaceae

Abiotrophia defectiva: nutritionally variant *Streptococcus* (requires pyridoxal); oral flora; causes endocarditis

Aerococcus: no growth at 45°C or 10°C; catalase negative, bile esculin, NaCl and PYR positive, no gas from glucose; susceptible to vancomycin

A.viridans: causes pseudobacteremia and, rarely, endocarditis and meningitis

Family Carnobacteriaceae

Granulicatella adiacens: nutritionally variant *Streptococcus* (requires pyridoxal); oral flora; causes endocarditis

G.balaenopterae: nutritionally variant *Streptococcus* (requires pyridoxal); oral flora; causes endocarditis

G.elegans: nutritionally variant *Streptococcus* (requires pyridoxal); oral flora; causes endocarditis

Family Enterococcaceae

Enterococcus: does not share close relationship with streptococci by DNA-RNA homology and differs from them in relative resistance to penicillin, high salt tolerance and cell wall antigens; Gram positive cocci in pairs or short chains; catalase negative; bile esculin, 6.5% NaCl and PYR positive; normal flora of mouth, tonsils, nose, large intestine, lower ileum, external genitalia, anterior urethra, vagina; causes bacteraemia and septicemia, asymptomatic bacteriuria, cerebrospinal fluid shunt infections, cholecystitis, acute cystitis, acute empyema, endocarditis, intraabdominal abscess, early neonatal meningitis, perinatal generalised disease, peritonitis (primary, secondary and continuous ambulatory peritoneal dialysis), pneumonia, postoperative complications, psoas abscess, pyelonephritis, 8% of nosocomial infections, infections in abnormal host (neutrophil dysfunction); selective adherence to endocardium; treatment: penicillin, amoxycillin or ampicillin (except in *E.faecium,* resistance not yet confirmed in Australia; 8% in USA) ± gentamicin or streptomycin, vancomycin; also susceptible to teicoplanin (0.06-0.5 mg/L), nitrofurantoin (2% resistance in USA); 100% intrinsic resistance to aminoglycosides, all cephalosporins, flucloxacillin, clindamycin; in Australia, 1% resistance to vancomycin (VanA: inducible by vancomycin or teicoplanin, vancomycin MIC > 256, teicoplanin MIC 16-256; VanB inducible by vancomycin only but exposure to vancomycin leads to teicoplanin resistance, vancomycin MIC 8-256, teicoplanin MIC 0.125-8; VanC constitutive, caused by chromosomally encoded genes (not transferable) found in all strains of *E.casseliflavis* and *E.gallinarum*, vancomycin MIC 4-16, teicoplanin MIC 0.125-8); < 5% β-lactamase producers in Australia

E.avium: group D; causes bacteraemia and septicemia in gastrointestinal tract abnormalities, infections in abnormal host; susceptible to ciprofloxacin (MIC 1 mg/L)

E.durans: β-haemolytic; group D; mannitol and sorbitol negative; causes infections in abnormal host; susceptible to amoxycillin-clavulanate (100% at 0.25 mg/L), cotrimoxazole (100% at 1 mg/L)

E.faecalis: β- or γ-haemolytic (rarely α); usually nonmotile; group D; bile esculin, 6.5% NaCl, glucose, salicin and mannitol positive; gelatine, catalase and nitrate negative; normal habitat gastrointestinal and genital tracts; causes abortional and puerperal infections, 0.5% of carpal tunnel syndrome, cholangitis and cholecystitis, endocarditis, gastroenteritis (rare), postneonatal pyogenic meningitis (infrequent in granulocyte disorders), peritonitis (rarely), acute pyelonephritis (rarely), septic arthritis, symbiotic gangrene, infections in abnormal host; treatment: vancomycin (0.4% resistance in Australia) or teicoplanin, penicillin or amoxy/ampicillin (0.7 % resistance in Australia) + gentamicin (12% high level resistance in Australia), amikacin, tobramycin or netilmicin; also susceptible to cotrimoxazole (MIC ≤ 0.06 mg/L), minocycline (0.2 mg/L), amoxycillin-clavulanate (100% at 0.5 mg/L), piperacillin, piperacillin-tazobactam, thienamycin (1 mg/L), imipenem, meropenem, linezolid, trimethoprim; variably susceptible to gatifloxacin, moxifloxacin; resistant to aminoglycosides (but synergy with cell wall active agent) and cephalosporins

E.faecium: group D; causes gastroenteritis (rare), infections in abnormal host; susceptible to cotrimoxazole (100% at ≤ 0.06 mg/L), amoxycillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, linezolid, synercid, trimethoprim; resistant to all cephalosporins, ciprofloxacin, enoxacin, norfloxacin; variably susceptible to gatifloxacin, moxifloxacin; in Australia, 69% resistant to ampicillin, 29% to gentamicin (high level), 7% to vancomycin; used as probiotic

Family Lactobacillaceae

Lactobacillus: Gram positive rods, no spores; nonmotile; facultative or obligate anaerobe; α- or γ-haemolytic (never β); growth at 10°C; glucose positive; H_2S not produced in triple sugar iron agar; catalase and nitrate negative; salicin, mannitol and bile esculin variable; lactic acid major or sole end-product of fermentation (propionic acid not produced); normal flora of mouth (usually present), saliva, colon and lower ileum (moderate to large numbers), urethra (irregular), vagina (large numbers), cervix (53-75%; sole or predominant organism in 46-66%); causes bacterial endocarditis (very rare; usually patients with preexisting structural heart disease and recent dental infection or manipulation), febrile disease (rare), lung abscess (extremely rare), 22% of anaerobic dental infections, 17% of anaerobic head and neck infections, 15% of transtracheal aspirates and pleural fluids growing anaerobes, 12% of anaerobic intraabdominal infections; treatment: penicillin ± gentamicin; 90% resistant to vancomycin

L.acidophilus: oral; causes endocarditis; used as probiotic

L.johnsonii: used as probiotic

L.paracasei: oral; causes endocarditis; used as probiotic

L.plantarum: oral; causes endocarditis; used as probiotic

L.reuterii: used as probiotic

L.rhamnosus: used as probiotic

L.salivarius: oral; causes endocarditis

Pediococcus: bile esculin positive, 6.5% NaCl variable, no gas from glucose, PYR negative, 95% react with streptococcal group D antiserum; resistant to vancomycin

Family Leuconostocaceae

Leuconostoc: catalase negative, produces gas from glucose, bile-esculin 90% positive, 6.5% NaCl variable; causes rare cases of bacteremia and septicemia associated with parenteral nutrition, other catheters and previous antimicrobial therapy; treatment: penicillin (MIC 1 mg/L), clindamycin; also susceptible to erythromycin (< 0.25 mg/L), cephazolin; resistant to vancomycin

Family Streptococcaceae

Lactococcus: growth at 10°C; no gas from glucose; susceptible to vancomycin

Streptococcus: Gram positive, cells round to slightly elongated, single and in short to long chains in liquid culture, may be encapsulated; adherence to blood agar and haemolysis variable; colonies small; growth in 5% NaCl, no growth in 6.5% NaCl, anaerobic growth in glucose variable; catalase negative; no gas from glucose; have no cytochromes; normal flora of vagina (25%), upper respiratory tract; causes abortional and puerperal infections, 15-20% of septic arthritis, 8% of brain and epidural abscess, acute bronchitis, bursitis, 2% of carpal tunnel syndrome, cat and dog bite infections, cholangitis and cholecystitis, purulent conjunctivitis, croup, dental caries (endogenous), 31-46% of endocarditis, acute epididymitis and epididymoorchitis, erysipelas, erythema nodosum, 22% of false aneurism, subacute febrile disease, emphysematous gastritis, impetigo, laryngotracheitis, local and generalised sepsis, mastitis and breast abscess, post-neonatal pyogenic meningitis, mycotic aneurism, 30% of necrotising fasciitis, osteomyelitis and osteochondritis, paronychia, perinatal generalised disease, peritonitis, pneumonia, pulmonary abscess, rhabdomyolysis, septicemia (in haemorrhagic fever), sore throat, symbiotic gangrene, symmetric peripheral gangrene, thyroiditis, tubo-ovarian abscess, vaginitis in prepubertal girls and elderly women, 2% of nosocomial infection, infections in abnormal host (neutrophil dysfunction); infection generally confined to epithelial surfaces; hemolysins (streptolysin O and S) induce lysosomal discharge into cell cytoplasm killing phagocyte, cause cell membrane lysis and also inhibit polymorph chemotaxis; M substance on fimbriae resists phagocytosis and digestion; C carboprotein protects from lysozyme; microbial antigens vary within host population; multiplies outside cells, but attachment to body surface necessary for invasion; fibrinolysin (streptokinase) and hyaluronidase cause spread of infection; growth stimulated by excess iron; primary immune defence prevention of attachment by coating microbial surface with specific antibody (mainly secretory IgA); neutralisation of microbial toxins also important; recovery from primary infection due to antibody; mean doubling time 20 minutes in vitro; treatment: penicillin (< 5% resistance in Australia), amoxycillin, ampicillin, clindamycin, erythromycin, roxithromycin, vancomycin (resistance not yet reported), amoxycillin-clavulanate; usually susceptible to oxacillin, cotrimoxazole, trimethoprim, chloramphenicol, cefotaxime, ceftriaxone, commonly susceptible to tetracycline; 100% intrinsic resistance to aminoglycosides because of thick peptidoglycan

S.agalactiae: β-hemolytic (also α, γ); group B; PYR negative; may be bacitracin susceptible; esculinase positive; normal flora of vagina, nasopharynx; causes amnionitis, bacteremia and septicemia (in neonates and hospitalised patients with underlying disease), asymptomatic bacteriuria, acute cystitis, cellulitis and pyomyositis (rare in diabetics), endocarditis (rarely), perinatal generalised disease, various diseases of neonate (abscess, endocarditis, meningitis, myocarditis, 40% of neonatal osteomyelitis, septicemia), neonatal and postneonatal pyogenic meningitis (≈ 100 cases/y in USA; 3-6% of bacterial meningitis; incidence 0.09/100 000 (42/100 000 at age < 1 mo); case-fatality rate 12-24%), peritonitis (primary and secondary), acute pharyngitis and exudative tonsillitis (mild and self-limiting), pneumonia, pyelonephritis, important cause of reproductive tract infections in women (chorioamnionitis, endometritis), local and generalised sepsis, septic abortion, septic arthritis (stage III prosthetic infection), 2% of surgical wound infections, toxic shock syndrome, urinary tract infections,

infections in abnormal host; mastitis in cow (attaches to duct epithelium); selective adherence to urogenital tissue; diagnosis: culture, coagglutination; treatment: penicillin (< 5% resistance in Australia), cefotaxime (≤ 0.06-0.25 mg/L), ceftriaxone; also susceptible to cefamandole (0.06 mg/L), erythromycin (0.06 mg/L), clindamycin (0.06 mg/L), meropenem (0.06 mg/L), ampicillin (0.12 mg/L), cefuroxime (≤ 0.25 mg/L), cotrimoxazole (100% susceptible at 0.25 mg/L), cefixime (≤ 0.25-1 mg/L), cefaclor (0.5 mg/L), ceftazidime (0.5 mg/L), mupirocin (0.5 mg/L), imipenem (100%), cefoxitin (100%), ampicillin (100%), amoxycillin, amoxycillin-clavulanate, vancomycin (resistance not yet reported), levofloxacin (2% resistance in USA); resistant to enoxacin, norfloxacin, amikacin, nalidixic acid, pefloxacin, gentamicin, tobramycin, neomycin, chloramphenicol, colistin, sulphamethoxazole; in Australia, 79% acquired resistance to tetracycline

S.anginosus: α-, β- or γ-hemolytic, minute colony; group C or F; trehalose and VP positive; sorbitol negative; oral flora; pathogenicity uncommon in animals, rare in humans; causes endocarditis

S.canis: β-hemolytic (also α, γ); group G; PYR negative; normal habitat nasopharynx, skin; causes acute glomerulonephritis (occasional), bacteraemia and septicemia (from cellulitis or abscess in patients with malignancies), cellulitis, endocarditis (rare), empyema, meningitis, osteomyelitis and osteochondritis (sacroilitis), otitis media, acute pharyngitis and exudative tonsillitis (mild and self-limiting), local and generalised sepsis, ulcers (rare), wound infections (rare); diagnosis: culture, coagglutination; susceptible to ceftizoxime (100% at ≤ 0.015 mg/L), imipenem (100% at ≤ 0.015 mg/L), penicillin (< 5% resistance in Australia), rifampicin (100% at 0.03 mg/L), ampicillin (100% at 0.06 mg/L), clindamycin (0.12 mg/L), azlocillin (100% at 0.125 mg/L), ceftazidime (0.125 mg/L), daptomycin (100% at 0.25 mg/L), cefotaxime (100% at 0.5 mg/L), ceftriaxone (100% at 0.5 mg/L), cefuroxime (100% at 0.5 mg/L), mezlocillin (100% at 0.5 mg/L), flucloxacillin (100% at 0.5 mg/L), cefazolin (100% at 1 mg/L), vancomycin (resistance not yet reported), cefoxitin (1 mg/L), netilmicin (1mg/L); resistant to enoxacin, norfloxacin

S.constellatus: microaerophilic; susceptible to novobiocin; resistant to metronidazole and SPS; produces lactic and acetic acids; oral flora; causes 2% of bacteremia and septicemia due to *'S.*viridans', endocarditis

S.cristatus: viridans group

S.dysagalactiae: α or γ hemolysis, large colonies; group C; trehalose positive; VP negative; sorbitol variable; causes mastitis in cow

S.equi subsp equi: β-hemolytic, large colonies; group C; VP, hippurate, trehalose and sorbitol negative; normal habitat nasopharynx, skin; causes bacteraemia and septicemia, infections in abnormal host, skin and wound infections (rare), endocarditis (rare), strangles in horse; susceptible to meropenem (MIC 0.03 mg/L)

S.equi subsp zooepidemicus: β-hemolytic, large colonies; group C; sorbitol positive; hippurate and trehalose negative; causes infections in horses, bacteremia and septicemia, endocarditis and rare foodborne outbreaks in humans

S.equinus: β- or γ-hemolytic (rarely α); no growth at 50°C; group D (non-enterococcus); lactose and starch positive, bile tolerant; causes bacteremia (possible indicator of colonic carcinoma), endocarditis, infections in abnormal host, urinary tract infections; treatment: penicillin or amoxycillin + gentamicin, netilmicin or streptomycin; may be tolerant to penicillin, oxacillin, ampicillin, cephalothin, vancomycin; also susceptible to amoxycillin-clavulanate (100% at 0.12 mg/L), cefaclor (100% at 0.25 mg/L), meropenem (0.25 mg/L), cotrimoxazole (100% at 0.5 mg/L), ciprofloxacin (1 mg/L), cefixime (1 mg/L)

S.equisimilis: β-hemolytic, large colonies; group C; trehalose positive; VP, hippurate, and sorbitol negative; produces streptokinase or streptolysin O; commonly pathogenic in humans (bacteremia and septicemia, endocarditis, rare cases of pneumonia secondary to tonsillitis and bronchitis), uncommonly in animals

S.gordonii: oral; causes endocarditis

S.iniae: causes invasive disease in fish grown in aquaculture and hand cellulitis and endocarditis in humans handling such fish

S.intermedius: part of *S.milleri* group; microaerophilic; susceptible to novobiocin; resistant to metronidazole and SPS; produces lactic and acetic acids; oral; causes 7% of bacteremia and septicemia due to *'S.viridans'*, endocarditis

S.milleri: group A, C, F, G or non-groupable; normal flora of teeth (28%), throat (31%), intestinal tract (15%), vagina (18%); causes abscesses, appendicitis, bacteraemia and septicemia (possible indicator of hidden abscess), brain abscess, cellulitis, cholangitis and cholecystitis, empyema, endocarditis, hepatic abscess, mouth abscess, osteomyelitis, pneumonia, parametritis, pelvic abscess, pelvic inflammatory disease, perinatal generalised disease, peritonitis (primary and secondary), sinusitis, surgical infections, wound infections; treatment: penicillin (< 5% resistance in Australia) or amoxycillin + surgery; also susceptible to meropenem (MIC 0.06 mg/L), vancomycin (resistance not yet reported)

S.mitis: lactose positive; starch negative; not bile tolerant; oral; selective adherence to buccal mucosa; adherence to nasal mucosa +; causes 41% of bacteremia and septicemia due to *'S.viridans'*, acute cystitis, endocarditis, perinatal generalised disease; susceptible to meropenem (MIC 1 mg/L)

S.mutans: viridans group; non-grouping; regular inhabitant of mouth; low adherence to nasal mucosa; causes 2% of bacteremia and septicemia due to *'S.*viridans', dental caries, endocarditis; initiates plaque on tooth by binding to glycosyltransferase, linked to glucan 'glue' (bacterial product), and attached to teeth

S.oralis: *S.sanguis* group; oral; causes endocarditis

S.parasanguis: *S.sanguis* group; causes endocarditis

S.pneumoniae: Gram positive, oval-shaped cocci in pairs or short chains; α- (rarely γ-) hemolytic; catalase negative; non-grouping; optochin susceptible; bile soluble; bile-esculin, NaCl and PYR negative; normal upper respiratory tract (mouth, nose, throat, tonsils) commensal (5-15% of adults without children, 38-65% of children 0-5 y, 60% of military personnel), can spread to infected or damaged lungs by autoinoculation or be transmitted via person-to-person contact by respiratory droplets; causes septic arthritis (52% of community acquired infections), 4-8% of bacteraemia and septicemia, brain abscess (occasional), bronchiectasis, acute bronchitis, acute bronchiolitis and bronchopneumonia, cellulitis (children, chronic illness, alcoholics, i.v. drug users), cervical fascial space infections, purulent conjunctivitis, croup, dacrocystitis, adenitis and canaliculitis, acute empyema, acute endocarditis, endometritis, endophthalmitis (septicemia), acute epiglottis (10% of adult cases), haemolytic uraemic syndrome, keratitis and iritis, laryngotracheitis, mastoiditis, early neonatal and post-neonatal meningitis ($\approx$ 500 cases/y in USA; 11-18% of bacterial meningitis; incidence 0.3/100 000 (8/100 000 at age 3-5 mo); case-fatality rate 19-28%), mycotic aneurism, nasal septal abscess, nasopharyngitis, 2% of osteomyelitis and osteochondritis, otitis media, pancreatic abscess, parametritis, pelvic abscess, pelvic inflammatory disease (IUD, recent birth, gynecologic surgery), pericarditis, perinatal generalised disease, peritonitis (primary and spontaneous), peritonsillar abscess, acute lobar pneumonia (36% of adult community-acquired and 50% of hospital-acquired), pulmonary abscess, preseptal and postseptal cellulitis, local and generalised sepsis (associated with connective tissue disorders), rhabdomyolysis, septicaemic adrenal haemorrhage syndrome, acute and chronic sinusitis, splenic abscess (rare), thyroiditis, vaginitis in infant girls, 0.6% of nosocomial infections (80% lower respiratory tract), infections in abnormal host (γ-globulin dysfunction, splenic dysfunction), systemic infection in agammaglobulinemia, C1, 2, 3, 4, factor B deficiency, hyposplenism/splenectomy; risk factors include < 2 y, Alaska native, African-American and American Indian children, cochlear implant, day care attendance, functional asplenia from sickle cell disease or splenectomy, immunosuppression (HIV, heukenia, lymphoma, malignancy, Hodgkin's disease, congenital disease, bone marrow transplantation, chemotherapy), > 65y, chronic cardiovascular disease (congestive heart failure, cardiomyopathy), chronic pulmonary disease (emphysema, chronic obstructive pulmonary disease, asthma with steroid use), chronic liver disease (cirrhosis), diabetes mellitus, chronic reanal insufficiency or renal failure, chronic CSF leakage from congenital lesions, neurosurgery or skull fracture, chronic systemic corticosteroids, cigarette smoking, alcoholism, homeless shelters, military training camps, prisons; case-fatality rate from 3% in bacteremic pneumococcal pneumonia in patients 14-29 y to 75% in extrapulmonary pneumococcal infection $\pm$ pneumonia in patients 70+ y; extracellular; polysaccharide capsule resists phagocytosis (unless antibody present) and digestion; type-specific polysaccharides associated with invasiveness (virulence factor); shows leucotoxicity; carried in blood free in plasma; microbial surface antigens in extracellular fluids combine with and 'divert' antibodies; hyaluronidase causes spread of infection; primary bodily defence mechanism humoral immune responses (β-lysin+, phagocytosis +, alternative complement +, immune adherence (phagocytosis) +++); diagnosis: counterimmunoelectrophoresis (antigen; type 14 not applicable due to neutral charge), smear and culture (CSF, sputum, body fluids), Quellung reaction, coagglutination, ELISA (sputum; sensitivity 96%, specificity 93%); susceptible to amoxy/ampicillin (in Australia, 6% resistance in hospitals and 2% in private laboratories), amoxycillin-clavulanate, cefaclor (MIC 0.5 mg/L), erythromycin (12% resistance in Australia), doxycycline/tetracycline (13% resistance in Australia), minocycline, roxithromycin (12% resistance in Australia), azithromycin, clarithromycin, penicillin (in Australia, 9% MIC $\geq$ 0.5 mg/L), cefotaxime (resistance not yet confirmed in Australia), ceftriaxone (< 1 mg/L), cefepime, vancomycin/teicoplanin (resistance not yet reported), cefmenoxime (0.01-0.06 mg/L), apalcillin ($\leq$ 0.02 mg/L), azlocillin ($\leq$ 0.02 mg/L), mezlocillin (< 0.02-0.25 mg/L), cefpiramide (0.02-0.25 mg/L), cefpirome (0.02-0.25 mg/L), clindamycin/lincomycin (< 0.06 mg/L), meropenem (0.06-1 mg/L), carbenicillin ($\leq$ 0.25 mg/L), ticarcillin ($\leq$ 0.25-1 mg/L), cefuroxime (0.5 mg/L), imipenem (100% at < 1 mg/L), meropenem, ceftizoxime (< 1 mg/L), cephalothin, cephazolin (< 1 mg/L), cefoperazone (< 1 mg/L), ceftazidime (< 1 mg/L), cefamandole (< 1 mg/L), piperacillin (1 mg/L), piperacillin-tazobactam, ticarcillin-clavulanate, mupirocin (1 mg/L), ofloxacin (1 mg/L), cefotetan, cefoxitin (100%), cephalexin, gatifloxacin, moxifloxacin, chloramphenicol (3% resistance in Australia), linezolid, synercid; in Australia, 80% resistance to cotrimoxazole, 52% resistant to trimethoprim

S.pyogenes: Gram positive cocci in chains; nonmotile; β-hemolytic (rarely α); group A; bacitracin susceptible (0.04 μg disc); resistant to 23.75 μg sulphamethoxazole + 1.25 μg trimethoprim disc; PYR, lactose, trehalose, glucose and salicin positive; hippurate, sorbitol, catalase, nitrate, esculin and mannitol negative; normal habitat nasopharynx (adherence to nasal mucosa +++), skin, rectum, female genial tract (low numbers; adherence to labium majus ++); causes many human diseases, including abortional and puerperal infections, appendicitis, bacteremia and septicemia, cellulitis (may be gangrenous or pyomyositis in diabetes), cervical adenitis, cranial fascial space infections, acute dacrocystitis, adenitis and canaliculitis, disseminated sepsis, acute empyema, endocarditis, endophthalmitis (septicaemic, posttraumatic), erysipelas, erythema marginatum (in 10% of cases of acute rheumatic fever), parametritis, pelvic abscess, pelvic inflammatory disease, perinatal generalised disease, glomerulonephritis (immunopathological basis; after pharyngitis or impetigo), impetigo, localised skin lesions, mastitis and breast abscess, postneonatal pyogenic meningitis, nasopharyngitis, otitis media, peritonsillar abscess, primary and secondary pneumonia (rarely; including diffuse interstitial pneumonia), pulmonary abscess, preseptal and postseptal cellulitis (secondary to puncture wounds or lacerations), purulent conjunctivitis, pyoderma (occasional in association with *Staphylococcus aureus*), rhabdomyolysis, rheumatic fever (immunopathological basis; after infection of upper

respiratory tract), scarlet fever (erythematous rash), local and generalised sepsis, septic arthritis (15% of total adult cases), septicaemic adrenal syndrome, acute and chronic sinusitis, sore throat, acute exudative tonsillitis, nonexudative pharyngitis and tonsillitis, acute tracheitis, 0.7% of surgical wound infections, chronic ulcers, vaginitis in prepubertal girls and elderly women, water-related infections (especially coral cuts), infections in abnormal host (interrupted integument, surgical procedure, neutrophil dysfunction), systemic infections in C1, 2, 3, 4, factor B deficiency, obsessive-compulsive disorder, attention deficit/hyperactivity disorder; 9600-9700 cases of invasive disease/y (1100-1200 deaths/y) in USA; binds to pharyngeal epithelium and skin via lipoteichoic acid on fimbriae (associated with invasiveness; virulence factor); adherence to nasal mucosa +++; extracellular; erythrogenic toxin (3 antigenic types) causes vasodilation, producing scarlet fever rash (stimulates production of inhibitory antibody); leucocidin and streptolysins (streptolysin O, but not streptolysin S, stimulates production of inhibitory antibody) kill phagocytes; steptokinase lyses fibrin, ? promoting spread of bacteria in tissues (virulence factor; stimulates production of inhibitory antibody); hyaluronidase liquefies connective tissue matrix, ? promoting spread of bacteria in tissues (virulence factor; stimulates production of inhibitory antibody); also produces haemolysins, streptodornase, NADase, DPNase (stimulates production of inhibitory antibody), proteinase (may stimulate production of inhibitory antibody), amylase (stimulates production of inhibitory antibody), esterases (do not stimulate production of inhibitory antibody), DNAse (stimulates production of inhibitory antibody); inhibits phagocytic attachment and ingestion; capsular hyaluronic acid and cell wall M (virulence factors, inhibit phagocytosis; anti-M protein antibodies confer specific immunity; hyaluronic acid not antigenic), T and R proteins and group-specific carbohydrates (A-rhamnose-N-acetylglucosamine) associated with invasiveness; acid shows leucotoxicity; kidney deposits of circulating immune complexes cause glomerulonephritis; major host defences β-lysin (+), phagocytes (+), alternative complement (+), interference with adherence (+), immune adherence (phagocytosis) (+++); protection depends on antibody against M protein; antibodies to various toxins do not prevent infection but may mitigate effects (eg., antierythrogenic toxin prevents rash of scarlet fever, antistreptokinase inhibits digestion of fibrin by streptokinase-plasminogen-plasmin system); diagnosis: indirect hemagglutination (Streptozyme™; ≥ 1:100), direct fluorescent antibody on throat swab, antistreptolysin O (≥ 166 Todd units, ≥ 170 IU), antideoxyribonuclease B (≥ 1:170), antihyaluronidase (≥ 1:256), throat swab culture, blood cultures, coagglutination, latex agglutination; susceptible to penicillin (resistance not yet reported), erythromycin (8% resistant in Australia), azithromycin, clarithromycin, roxithromycin, clindamycin, lincomycin, amoxycillin, cefotaxime (< 1 mg/L), ceftriaxone (< 1 mg/L), cefepime, di/flucloxacillin, cephalothin, vancomycin/teicoplanin (resistance not yet reported), cephalexin (0.5-1 mg/L), sulphadiazine, imipenem (0.008 mg/L), meropenem (≤ 0.01 mg/L), cefmenoxime (0.01-0.03 mg/L), apalcillin (≤ 0.02 mg/L), azlocillin (≤ 0.02 mg/L), mezlocillin (≤ 0.02-0.25 mg/L), piperacillin (≤ 0.02-0.25 mg/L), piperacillin-tazobactam, cefpiramide (0.02-0.25 mg/L), cefpirome (0.02-0.25 mg/L), amoxycillin-clavulanate (100% at ≤ 0.06 mg/L), cotrimoxazole (≤ 0.06-1 mg/L), cefotetan (≤ 0.12 mg/L), mupirocin (0.12 mg/L), oxacillin (≤ 0.25 mg/L), ampicillin (≤ 0.25 mg/L), cefuroxime (≤ 0.25 mg/L), carbenicillin (≤ 0.25-1 mg/L), ticarcillin (≤ 0.25-1 mg/L), ticarcillin-clavulanate, ceftazidime (0.25 mg/L), cefaclor (100% at 0.5 mg/L), cefixime (< 1 mg/L), ceftizoxime (< 1 g/L), ceftazidime (< 1 mg/L), cefoperazone (< 1 mg/L), cefoxitin (< 1 mg/L), cefamandole (< 1 mg/L), cephazolin (< 1 mg/L), tetracyclines (1 mg/L), trimethoprim, gatifloxacin, moxifloxacin, sodium fusidate, linezolid, synercid, rifampicin, rifabutin, trimethoprim, cotrimoxazole, usually susceptible to chloramphenicol

S.salivarius: viridans group; no growth at 50°C; group K; lactose positive; starch negative; not bile tolerant; oral; binds to buccal epithelium and tongue via ? lipoteichoic acid on fimbriae or ? lipoprotein fibrillar coat; adherence to nasal mucosa +; causes 2% of bacteremia and septicemia due to '*Streptococcus viridans*', endocarditis, infections in abnormal host

S.sanguis: viridans group; group H; oral; selective adherence to teeth; causes 22% of bacteraemia and septicemia due to '*Streptococcus viridans*', brain abscess in intermittently treated jaw infections, endocarditis (fibronectin binding important factor), infections in abnormal host; IgA proteases interfere with IgA1; treatment: penicillin; also susceptible to ciprofloxacin (MIC 0.25 mg/L), meropenem (1 mg/L)

S.sobrinus: viridans group

S.suis: groups R and S but cross-reacts with group D; causes postneonatal pyogenic meningitis in pig workers; treatment: penicillin, cefotaxime, ceftriaxone

S.uberis: group E; causes mastitis in cattle

S.vestibularis: viridans group

S.viridans: α-hemolytic; bile esculin, NaCl and PYR negative; normal flora of skin, mouth, throat, large intestine, lower ileum, external genitalia (adherence to labium majus +), anterior urethra (rare), vagina, eye; does not adhere to nasal mucosa; oral commensals settle on abnormal heart valves during bacteaemia (dextran important factor); causes appendicitis, 3-5% of bacteremia and septicemia, cholangitis and cholecysitis, 50-70% of subacute bacterial endocarditis cases, endophthalmitis (conjunctival filtering-bleb associated, bloodborne), keratitis and iritis, osteomyelitis and osteochondritis, perinatal generalised disease, peritonitis in continuous ambulatory peritoneal dialysis, psoas abscess, acute and chronic sinusitis, subacute febrile disease; susceptible to penicillin, amoxy/ampicillin, amoxycillin-clavulanate,, erythromycin (MIC < 0.06 mg/L), azithromycin, clarithromycin, roxithromycin, clindamycin (< 0.06 mg/L), lincomycin, vancomycin/teicoplanin (resistance reported in USA and Europe), cefotaxime (0.5 mg/L), ceftriaxone, cefepime, cefpirome,

ceftazidime, piperacillin (0.5 mg/L), piperacillin-tazobactam, ticarcillin-clavulanate, cephalexin, cephalothin, cephazolin, cefaclor, cefuroxime, cefotetan, cefoxitin (100%), imipenem (100%), meropenem, gatifloxacin, moxifloxacin, chloramphenicol, linezolid, synercid

Group C *Streptococcus*: *S.dysagalactiae, S.equi, S.equisimilis* (also some *S.milleri*); hemolysis variable; PYR negative; cause bacteremia and septicemia in cardiovascular disease and malignancy, endocarditis, acute epiglottitis (1 case), acute pharyngitis, acute exudative tonsillitis, acute and chronic sinusitis, pneumonia (rare), local and generalised sepsis, cellulitis, impetigo, myocarditis and pericarditis (rare), perinatal generalised disease, post-streptococcal glomerulonephritis (occasional), neonatal meningitis, 0.8% of otitis externa, septic arthritis, osteomyelitis and osteochondritis, many animal diseases; most infections in man due to *S.equisimilis*; treatment: penicillin (< 5% resistance in Australia), flucloxacillin, erythromycin; 100% susceptible to vancomycin, ciprofloxacin, imipenem; resistant to enoxacin

Group D '*Streptococcus*': *Enterococcus, S.equinus*; hemolysis variable; bile esculin positive; dairy products, intestinal tract of man and animals; cause bacteremia and septicemia, endocarditis, local and generalised sepsis, neonatal sepsis, nosocomial infection, perianal and perirectal abscess and cellulitis in patients with malignant disease, pelvic abscess, perinatal generalised disease, peritoneal abscess, septic endometritis, septic meningitis, septic thrombophlebitis, 10% of surgical wound infections, urogenital infection; diagnosis: culture, coagglutination; treatment: penicillin or ampicillin + gentamicin

Group E *Streptococcus:* hemolytic; cause pharyngeal abscesses in swine

Group F *Streptococcus:* some *S.milleri*; hemolytic; PYR negative; found in respiratory tract; susceptible to penicillin (< 5% resistance in Australia), vancomycin (resistance not yet reported)

Group G *Streptococcus:* *S.canis* and some *S.milleri*; hemolytic; cause mild respiratory infections and occasional post-streptococcal glomerulonephritis in man, rare genital infections in dogs; susceptible to meropenem (MIC 0.03 mg/L)

Group H *Streptococcus*: hemolysis variable; found in respiratory tract of man

Group K *Streptococcus*: hemolysis variable; found in respiratory tract of man

Group L *Streptococcus*: hemolytic; cause more invasive vaginitis in dogs

Group M *Streptococcus*: hemolytic; non-pathogen in dog's vagina

Group N *Streptococcus*: non-hemolytic; dairy foods

Group O *Streptococcus*: hemolysis variable; carried in upper respiratory tract of man; cause endocarditis

Class Clostridia

Order Clostridiales

Family Clostridiaceae

Clostridium: Gram positive sporebearing (sometimes difficult to demonstrate) bacillus, typically large straight rods, may be pleomorphic, can rapidly lose their Gram stain; motile; most species only anaerobic growth; catalase negative; normal flora of colon and lower ileum (large numbers), mouth, urethra and vagina (irregular); widely distributed in soil; causes abortional and puerperal infection, 1-2% of bacteremia and septicemia, botulism, cellulitis, cholecystitis, choledochitis, complication of surgical procedures, food poisoning, gas gangrene (myonecrosis), intraabdominal abscess, ischiorectal abscess, postneonatal pyogenic meningitis (infrequent), peritonitis, pseudomembranous colitis, rhabdomyolysis, local and generalised sepsis, tetanus, wound infection; growth stimulated by excess iron; treatment: penicillin (100% susceptible), chloramphenicol (100% susceptible), metronidazole (99% susceptible), clindamycin (88-90% susceptible), cefoxitin, erythromycin; also susceptible to mezlocillin (100% at $\leq$ 1 mg/L), imipenem (100%), ampicillin-sulbactam (100%), piperacillin (100%), ticarcillin-clavulanate (100%), ticarcillin (100%), cefotetan (95-100%), cefoperazone (84-100%), ceftizoxime (75-100%), moxalactam (73-100%), carbenicillin; resistant to ciprofloxacin, ofloxacin, lomefloxacin, enoxacin, cefotaxime, cefmenoxime, gentamicin

C.bifermentans: spores subterminal; nonmotile; hemolytic, no aerobic growth; fructose, esculin, indole, lecithinase, gelatinase, glucose, maltose, indole positive; lactose and sucrose negative; milk clot and digestion; acetic, propionic, isobutyric, isovaleric, isocaproic acids by GLC; nontoxic to mice; susceptible to meropenem (MIC 0.13 mg/L)

C.botulinum: oval, subterminal spores, no capsule; nonmotile; no aerobic growth; glucose positive; lecithinase and indole negative; proteolysis, maltose, lactose, sucrose and milk reaction variable; exotoxin^{+++}; toxic to mice; toxin neutralisation for specific identification; causes botulism (food (enterotoxemia; 66% type A, 5% type B, 25% type E), infant, wound), localised skin lesions, local and generalised sepsis, pneumonia, osteomyelitis and osteochondrtitis (in wound botulism), sudden infant death syndrome; powerful neurotoxin (exotoxic protein) absorbed from intestine (incubation period 5-36 h) blocks release of acetylcholine, causing neurotoxic signs and paralyses; 6 types (A (USA, former Soviet Union; proteolytic; botulism of man, limberneck of chickens), B (USA, Northern Europe, former Soviet Union; some strains proteolytic; botulism of man, limberneck of chickens), C (nonproteolytic; paralytic disease of chickens, botulism of wild animals, forage poisoning of cattle in Australia), D (nonproteolytic; Lamzochte of cattle in Africa), E (Northern Europe, Canada, USA, Japan, former Soviet Union; nonproteolytic; botulism of man), F (Denmark, USA; proteolytic; botulism of man)) produce immunologically distinct toxins; diagnosis can be performed by demonstrating toxin in blood; treatment: antitoxin (confers specific immunity and is of proven value in treatment), tetracycline, metronidazole, chloramphenicol, penicillin, clindamycin

C.butyricum: causes necrotising enterocolitis; susceptible to meropenem (MIC 0.5 mg/L)

C.chauvoei: causes blackleg in cattle, horses, pigs, sheep

C.difficile: spores subterminal; motile; no aerobic growth; yellow colonies (usually flat and dull) with spreading, irregular or rhizoid edge, fluorescing bright yellow under long wavelength UV light, on cycloserine cefoxitin egg yolk fructose agar; colonies on blood agar nonhaemolytic, fluoresce yellow-green under long wavelength UV light; very characteristic 'horse stable' odour; fructose, esculin and glucose positive; milk digestion, indole, lecithinase, lactose, maltose and sucrose negative; gelatinase variable; acetic, propionic, isobutyric, butyric, isovaleric, valeric, isocaproic acids by GLC; toxin neutralisation for specific identification; causes reactive arthritis, bacteraemia and septicemia in immunocompromised, acute diarrhoea and/or vomiting, pseudomembranous colitis (caused by necrotising action of toxin on colonic mucosa; complication of antimicrobial therapy (clindamycin and amoxycillin most frequent) causing overgrowth of *C.difficile*, 4% of faecal specimens (up to 44% in neonates), causes 11% of enteritis, 15-52% of nosocomial diarrhoea; attack rate 32% in day care centres), splenic abscess, ? ulcerative colitis; treatment: metronidazole/tinidazole (MIC < 1 mg/L), vancomycin/teicoplanin (oral), bacitracin (oral), cholestyramine

C.fallax: causes gas gangrene, cellulitis, myonecrosis; treatment: clindamycin, metronidazole, penicillin, erythromycin

C.histolyticum: oval, subterminal spore, no capsule; motile; aerobic and anaerobic growth; proteolytic, milk clot and digestion, gelatinase positive; glucose, lactose, maltose, sucrose, indole and lecithinase negative; acetic, lactic acids by GLC; exotoxin positive; toxicity to mice variable; causes 0.8% of carpal tunnel syndrome

C.novyi: oval, subterminal spores; motile, no capsule; no aerobic growth; slight proteolysis; glucose^{+}, lecithinase^{+} and gelatinase positive; lactose, sucrose and indole negative; maltose and milk variable; acetic, propionic, butyric acids by GLC; exotoxin +++; toxicity to mice variable; toxin neutralisation for specific identification; causes cellulitis, myonecrosis with rapid progressive tissue death (sometimes associated with production of gas in tissues), gas gangrene, bacteremia and septicemia in immunocompromised, black disease of cattle, horses, pigs and sheep; α toxin (lethal, necrotising) produced by types A and B, β toxin (hemolytic, necrotising, lecithinase), γ toxin (hemolytic, lecithinase), δ toxin (CO_2-labile hemolytic) and ε toxin (opalescence in lecithovitellin) by type A, ξ toxin (hemolytic) by type B; treatment: clindamycin, metronidazole, penicillin, erythromycin

C.perfringens: large Gram positive bacillus with square ends, oval subterminal spores with no swelling, encapsulated; nonmotile; only anaerobic growth; complex nutritional requirements, optimal temperature 43-45°C; double zone of haemolysis; Nagler positive; liquefies gelatine, slight proteolysis; glucose, lactose, maltose, sucrose, and lecithinase positive; indole negative; milk clot and gas; acetic, butyric acids by GLC; exotoxin^{++}; toxicity to mice variable; normal flora of colon; causes abortional infection, 6% of anaerobic bacteremia and septicemia, cellulitis, cholangitis and cholecystitis, compound fractures infections, acute empyema (rare), enterotoxemia, Darmbrand, necrotising enterocolitis, gastroenteritis (uncommon), gas gangrene, myonecrosis with rapid progressive tissue death, postoperative gangrene (usually arising from intestine), parametritis, pelvic abscess, pelvic inflammatory disease, perinatal generalised disease, peritonitis, rhabdomyolysis, 15% of anaerobic intraabdominal infections in humans, necrotising enterocolitis and pulpy kidney disease in calves, piglets, foals and lambs (type D); all types produce α toxin (lethal, lecithinase, necrotising, phospholipase; acts on cell membrane of muscle, causing cell necrosis, haemolysis, toxaemia, capillary fragility), κ toxin (collagenase; destroys collagen framework in intact muscle), μ toxin (hyaluronidase; depolymerises hyaluronic acid in intercellular ground substance), and η toxin (deoxyribonuclease); antibodies to phospholipase, but not collagenase and hyaluronidase, protective against infection; capsule resists phagocytosis; diagnosis: culture, ELISA (toxin); susceptible to benzylpenicillin (a few strains resistant), phenoxymethylpenicillin, amoxy/ampicillin, clindamycin (MIC < 1 mg/L), lincomycin, metronidazole/tinidazole (99% susceptible), erythromycin, meropenem ($\leq$ 0.06 mg/L), cephalexin, cephalothin, cephazolin, cefaclor, cefuroxime, cefotaxime, ceftriaxone, cefepime, cefpirome, ceftazidime, cefotetan ($\leq$ 0.12 mg/L), cefoxitin, ciprofloxacin ($\leq$ 0.13-0.5 mg/L), ofloxacin ($\leq$ 0.25-0.5 mg/L), pefloxacin ($\leq$ 0.25-1 mg/L), ticarcillin ($\leq$ 1 mg/L), ticarcillin-clavulanate ($\leq$ 1 mg/L), piperacillin (1 mg/L), piperacillin-tazobactam, ticarcillin-clavulanate, imipenem (99% at 1 mg/L), meropenem, chloramphenicol, vancomycin, teicoplanin, carbenicillin, gatifloxacin, moxifloxacin, azithromycin, clarithromycin, erythromycin, roxithromycin; antitoxin of no proven value in treatment

C.perfringens A: causes food poisoning; ubiquitous organism, resists heat of cooking and multiplies in anaerobic conditions (eg., bulky meat and poultry dishes, pies and stews), limited multiplication and production of enterotoxin during spore formation, enterotoxin released in gut causing abdominal pain and diarrhoea, incubation period 9-24 h, disease-producing dose 10^8 organisms, transmitted by food and water; some strans produce θ toxin (oxygen-labile hemolysin; inhibits chemotaxis, hemolytic, necrotising)

C.perfringens B: produces β toxin (lethal, necrotising, may be neurotoxic), ε toxin (lethal, affects gut permeability, necrotising)

C.perfringens C: causes pigbel (oxygen-labile haemolysin, collagenase and hyaluronidase-producing strains); produces β toxin (lethal, necrotising, may be neurotoxic),

C.perfringens D: produces ε toxin (lethal, affects gut permeability, necrotising)

C.perfringens E: produces ι toxin (lethal, affects capillary permeability, necrotising);

C.septicum: oval subterminal spores, no capsule; motile; no aerobic growth; heavy swarming; slight proteolysis; glucose, lactose, maltose, gelatinase positive; sucrose, indole and lecithinase negative; milk clot and gas; acetic, butyric acids by GLC; exotoxin^{++}; toxic to mice; toxin neutralisation for specific identification; causes 2% of anaerobic bacteraemia and septicemia, cellulitis, myonecrosis with rapid progressive tissue death (sometimes associated with production of gas in tissues), blackleg in cattle, horses, pigs and sheep; treatment: clindamycin, metronidazole, penicillin, erythromycin; also susceptible to meropenem (MIC 0.06 mg/L)

C.sordellii: hemolytic; urease, indole and lecithinase positive; esculin and milk digestion negative; infections following trauma, childbirth, routine gynecological procedures, medically induced abortions, injection drug use; overall case fatality rate 69%; susceptible to meropenem (MIC 0.06 mg/L)

C.sporogenes: spores subterminal; motile; no aerobic growth; milk clot and digestion; gelatinase and sucrose positive; lecithinase, lactose and indole negative; maltose variable; isovaleric acid by GLC; nontoxic to mice; susceptible to meropenem (MIC 0.25 mg/L)

C.tertium: Gram positive bacillus with oval terminal spore; motile; both aerobic and anaerobic growth; lactose, glucose, maltose and sucrose positive; lecithinase, gelatinase and indole negative; action on milk variable; acetic, butyric, lactic acids by GLC; nontoxic to mice; causes 13% of anaerobic bacteremia and septicemia (neutropenics and aspiration pneumonia)

C.tetani: 'drum stick' appearance, with large terminal spherical spore; noncapsulated; motile; no aerobic growth; heavy swarming; nonproteolytic; milk no change; gelatinase positive; glucose, lactose, sucrose and lecithinase negative; indole variable; acetic, propionic, butyric acids by GLC; exotoxin^{+++}; toxic to mice; toxin neutralisation for specific identification; causes tetanus; non-invasive; toxin (exotoxic protein) is bound by ganglioside of nervous tissue and blocks action of inhibitory neurones, causing overaction of motor neurones, producing muscle spasm, lockjaw; antitoxin protective; treatment: immunoglobulin or antitoxin + penicillin or cephalosporin or erythromycin

Sarcina: normal flora of large intestine, external genitalia, vagina (2%), skin; causes complications in compromised patients, postpartum or postoperative complications (rare); isolated from diseased stomach

Clostridiales Family XI Incertae Sedis

Anaerococcus hydrogenalis: has been isolated from vaginal discharge

A.lactolyticus: new species

A.prevotii: indole negative, resistant to novobiocin, produces butyric and acetic acids; skin, vagina, tonsils; susceptible to ticarcillin (MIC $\leq$ 1 mg/L)

A.tetradius: glucose and urease positive; lactose negative; produces butyric and lactic acids; vagina, vaginal discharge and various purulent secretions

Finegoldia

Peptostreptococcus magnus: large cocci; glucose and lactose negative, resistant to novobiocin, produces acetic acid; oral, genital tract, rare in colon or gingival crevice; causes endocarditis, wounds, abscesses of abdomen, peritoneal, appendiceal or gingival sites, perinatal generalised disease; more frequent in anatomic sites below diaphragm; treatment: penicillin; also susceptible to meropenem (MIC 0.13 mg/L)

Parvimonas micra: small cocci; glucose and lactose negative, susceptible to novobiocin; produces acetic acid; genital tract, frequently in healthy gingival crevice and intestinal tract; frequently isolated from clinical specimens, including brain, lung, jaw, head, neck and bite abscesses, spinal fluid, blood and abscesses at other body sites; often a major component of flora of gingival sulcus in periodontal disease; susceptible to meropenem (MIC 0.25 mg/L)

Peptoniphilus indolicus: most biochemical properties as for *Peptostreptococcus ascaccharolyticus*

P.lacrimalis: new species

Peptostreptococcus asaccharolyticus: SPS resistant, indole positive, produces butyric acid; vagina; vaginal discharge, skin abscess, peritoneal abscess; susceptible to meropenem (MIC 0.03 mg/L), ticarcillin ($\leq$ 1 mg/L), ticarcillin-clavulanate ($\leq$ 1 mg/L)

Tissierella praeacuta: normal flora of gastrointestinal tract; causes bone and soft tissue infection, intraabdominal abscess, peritonitis; susceptible to cefamandole (MIC $\leq$ 0.062 mg/L), cefoxitin ($\leq$ 0.062 mg/L), moxalactam ($\leq$ 0.062 mg/L), clindamycin ($\leq$ 0.062 mg/L), erythromycin ($\leq$ 0.062 mg/L)

Family Eubacteriaceae

Eubacterium: Gram positive rod, regular and irregular, nonsporeforming, non-acid fast; motility variable; smooth colonies on blood agar, diffuse growth in enriched thioglycolate broth; catalase and indole negative; normal flora of mouth (usually present) and upper respiratory tract (irregular), vagina (irregular), large intestine (large numbers), skin (irregular); also animal, soil; causes diverticulitis, chronic mastitis and breast abscess, peritonitis, 37% of anaerobic intraabdominal infections, 25% of head and neck infections, pulmonary abscess (23% of transtracheal aspirates and pleural fluids growing anaerobes), 18% of anaerobic animal bite infections, 18% of perirectal abscess, 16% of anaerobic miscellaneous soft tissue infections below waist, 13% of decubitus ulcers, 12% of foot ulcers, 11% of dental infections, 11% of anaerobic miscellaneous soft tissue infections above waist; often associated with necrotising pneumonia; treatment: penicillin, tetracycline; 100% susceptible to imipenem; resistant to ciprofloxacin

E.limosum: plump rods, bulbous and bifid forms; glucose fermented; metabolic products acetic, butyric acids
E.sulci: new species
E.tenue: causes trichomycosis axillaris; diagnosis: microscopy of hair; treatment: shaving, sulphur ointment
E.yurii: new species
E.yurii subsp margaretiae: new subspecies
E.yurii subsp schtitka: new subspecies
E.yurii subsp yurii: new subspecies
Pseudoramibacter alactolyticus: thin rods, V forms, cross-stick arrangements; ferments glucose; produces acetic, butyric, caproic acids

Family Lachnospiraceae

Butyrivibrio fibrisolvens: anaerobic, Gram negative bacillus, nonsporeforming, motile by polar flagella, fermentative, butyric acid produced; normal flora of large intestine; single case of endophthalmitis following penetrating injury; susceptible to penicillin, chloramphenicol, erythromycin, tetracycline; resistant to bacitracin, streptomycin, kanamycin, lincomycin, sulphonamides
Coprococcus: 3 species isolated from feces but not from clinical specimens
Lachnospira: propionic acid not produced, ratio of lactic to acetic acid produced < 1:1, produces butyric acid and other acids or no major acid

Family Peptococcaceae

Peptococcus: causes peritonsillar abscess, necrotising pneumonia, pulmonary abscess, tubo-ovarian abscess, endometritis, local and generalised sepsis, cellulitis, 0.4% of bacteraemia and septicemia (mainly obstetrical patients during peripartum period); treatment: chloramphenicol, metronidazole
P.niger: obligately anaerobic Gram positive coccus, cells singly or in clumps; susceptible to metronidazole; resistant to novobiocin and SPS; indole negative; butyric, caproic, isovaleric and acetic acids produced; normal flora of external genitalia, cervix (7-71%), vagina, skin (umbilicus), tonsils, throat, mouth, large intestine; only occasionally isolated from human clinical specimens; more commonly isolated from veterinary specimens; causes complications in compromised patients, infections in abnormal host, lung abscess (rare), myonecrosis, peritonitis, postpartum or postoperative complications, various abscesses; susceptible to metronidazole (MIC 1 mg/L), imipenem (100%)

Family Peptostreptococcaceae

Peptostreptococcus: obligately anaerobic Gram positive coccus, cells in chains, γ-haemolytic; normal flora of external genitalia, cervix (14-33%), vagina (19%), colon, lower ileum, mouth, tonsils, skin; causes abortional and puerperal infections, abscesses (including brain abscess, peritonsillar abscess, lung abscess; in pure culture or as part of mixed aerobic and anaerobic flora), 1% of bacteraemia and septicemia (8% of septicemia associated with female genital infection), cholecystitis, cervical fascial space infections, cranial parameningeal deep fascial space infection, empyema, gangrene (including Fournier's gangrene of scrotum and lung gangrene), chronic mastitis and breast abscess, osteomyelitis and osteochondritis, chronic otitis externa, pleuritis, necrotising pneumonia, sinusitis, tubo-ovarian abscess, infections in abnormal host, ≈ 100% of anaerobic dental infections, decubitus ulcers, foot ulcers and osteomyelitis, 98% of anaerobic miscellaneous soft tissue infections below waist, 68% of pancreatic abscess, 62% of miscellaneous soft tissue infections above waist, 51% of intraabdominal infections, 40% of human bite infections, 33% of transtracheal aspirates and pleural fluids growing anaerobes, 21% of anaerobic CNS infections, 21% of animal bite infections; treatment: benzylpenicillin (most reliable antimicrobial for treating bacteraemia), chloramphenicol, metronidazole/tinidazole (MIC 1 mg/L), clindamycin/lincomycin; also susceptible to phenoxymethylpenicillin, amoxy/ampicillin, amoxycillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, cefaclor, cefuroxime, cefotaxime, ceftriaxone, cefepime, cefpirome, cefotetan (MIC 0.5 mg/L), cefoxitin, imipenem (100%), meropenem, gatifloxacin, moxifloxacin, azithromycin, clarithromycin, erythromycin, roxithromycin, vancomycin, teicoplanin
P.anaerobius: produces acetic and isocaproic acids, susceptible to sodium polyanethol sulphonate; vagina, colon; isolated from a wide variety of clinical specimens, including abscesses of brain, jaw, pleural cavity, ear, pelvic region, urogenital area and abdominal region; also from blood, spinal fluid, joint cultures and specimens from osteomyelitis, gingival crevice of persons with gingivitis or periodontal disease

Family Ruminococcaceae

Ruminococcus bromii: normal flora of large intestine; isolated from feces but not from clinical specimens
R.productus: glucose and lactose positive, produces acetic acid; colon (1 of more predominant members of fecal flora)

Family Veillonellaceae

Acidaminococcus fermentans: obligately anaerobic Gram negative cocci, produces butyric and acetic acids; nitrate negative; normal flora of large intestine; rarely isolated from clinical specimens
Anaerovibrio: motile by polar flagella, anaerobic, Gram negative bacillus, fermentative, propionic and acetic acids produced
Centipeda periodontii: new genus and species

Dialister pneumosintes: bacilli ≤ 0.3 μm length; normal flora of nasopharynx and oropharynx, gastrointestinal tact, cervix, vagina; causes chronic disease of meninges and other organs (rare), pneumonia; treatment: metronidazole; also susceptible to ampicillin (MIC 0.25 mg/L)

Megamonas hypermegale: normal flora of gastrointestinal tract

Megasphaera elsdenii: nitrate negative; colon; rarely isolated from clinical specimens

Mitsuokella multiacida: normal flora of gastrointestinal tract

Selenomonas sputigena: obligately anaerobic, Gram negative rods, motile by tuft of flagella on concave side of crescent-shaped cells, fermentative metabolism; normal flora of nasopharynx, oral cavity; causes sepsis (in alcoholism), lung abscess; susceptible to clindamycin, chloramphenicol, metronidazole; resistant to vancomycin, colistin

Veillonella: anaerobic Gram negative cocci resembling *Neisseria*; pink to red fluorescence under ultraviolet light (360 nm); produces propionic acid; nitrate positive; susceptible to erythromycin, rifampicin, colistin, penicillin, kanamycin; resistant to vancomycin; normal flora of cervix (27%), vagina, mouth, tonsils, large intestine; causes bacteraemia and septicemia, endocarditis (polymicrobial), cranial parameningeal deep fascial space infections, infections in abnormal host, 44% of anaerobic human bite infections, 33% of anaerobic head and neck infections, 33% of anaerobic dental infections, 26% of transtracheal aspirates and pleural fluids growing anaerobes, 12% of perirectal abscess, 11% of anaerobic miscellaneous soft tissue infections above waist; usually found with other aerobes and anaerobes, role in infection remains uncertain; 100% susceptible to imipenem

V.parvula: found in mouths of many healthy persons; may on rare occasions act as opportunistic pathogen, causing abscesses, cat and dog bite infections, osteomyelitis and osteochondritis, wound infections and respiratory tract disease (pneumonia), endocarditis (polymicrobial); treatment: chloramphenicol, clindamycin

Class Erysipelotrichi

Order Erysipelotrichales

Order Erysipelotrichaceae

Erysipelothrix: resembles *Listeria* but catalase negative and filamentous; growth stimulated by excess iron

E.rhusiopathiae: diphtheroid-appearing rod; non-motile; α-hemolytic (never β-hemolytic) on blood agar; H_2S in triple sugar iron agar, glucose positive; catalase, nitrate, esculin, maltose, sucrose, salicin and mannitol negative; causes arthritis, cellulitis, conjunctivitis without keratitis, endocarditis (animal contact, alcohol abuse), erysipeloid and bacteraemia and septicemia in humans, and cutaneous disease (diamondback, diamond skin infection, swine erysipelas), acute septicemia and arthritis in pigs; transmitted from animals to humans; treatment: penicillin (100% susceptible at 0.06 mg/L), erythromycin (100% susceptible at 0.25 mg/L); also susceptible to cloxacillin (100% at 0.025 mg/L), methicillin (100% at ≤ 0.12 mg/L), flucloxacillin (100% at ≤ 0.12 mg/L), tetracycline (MIC 0.2 mg/L; MBC 16-31 mg/L), ampicillin (100% at 0.25 mg/L), clindamycin (100% at 0.25 mg/L), cephalothin (100% at 1 mg/L); resistant to sulphonamides, cotrimoxazole, vancomycin, aminoglycosides

Unclassified Erysipelotrichaceae

Clostridium innocuum: spores terminal; nonmotile; colonies on cycloserine cefoxitin fructose agar similar to *C.difficile* but slightly umbonate and glistening; colonies on blood agar not fluorescent; no odour

Lactobacillus catenaformis: short rods in chains or singly; smooth colonies on blood agar, diffuse granular growth in enriched thioglycolate broth; obligate anaerobe; catalase and indole negative, glucose fermented (metabolic products acetic and lactic acids)

Streptococcus pleomorphus: colon

Phylum Fusobacteria

Class Fusobacteria

Order Fusobacterales

Family Fusobacteriaceae

Fusobacterium: strictly anaerobic Gram negative long thin cells with tapered ends, nonsporeforming, motile by peritrichous flagella or nonmotile; produces butyric acid without much isobutyric or isovaleric acids; vancomycin resistant, kanamycin susceptible, colistin susceptible; normal flora of mouth (large numbers), tonsils (usually present), large intestine (irregular), lower ileum (irregular), external genitalia (usually present), urethra (usually present), vagina (irregular); causes abscesses, 0.3% of bacteraemia and septicemia, complication of cat and dog and human bite and clenched fist injuries, acute empyema, lung abscesses, intraabdominal abscess, peritonsillar abscess, cranial parameningeal deep fascial space infections; susceptible to metronidazole/tinidazole (100% at < 1 mg/L), chloramphenicol (100%), penicillin (100%), cefoxitin (99%), ampicillin-sulbactam (97%), ticarcillin-clavulanate (97%), ceftizoxime (94-100%), clindamycin/lincomycin (92%), cefotaxime/ceftriaxone (90-100%), piperacillin (85-99%), amoxy/ampicillin, amoxycillin-clavulanate, piperacillin-tazobactam, ticarcillin-clavulanate, cephalexin, cephalothin, cephazolin, cefaclor, cefuroxime, cefepime, ceftazidime, cefotetan, imipenem, meropenem, azithromycin, clarithromycin, erythromycin, roxithromycin; resistant to fluoroquinolones

F.gonidiaformans: gas, indole and threonine positive; esculin and lactate negative

F.mortiferum: gas, bile-esculin and threonine positive; indole, lactate and lipase negative; erythromycin and rifampicin resistant

F.naviforme: gas and indole positive; esculin, threonine and lactate negative

F.necrophorum: usually β-hemolytic, sometimes α; ≥ 20 mm zone of inhibition with 2U penicillin disc, ≥ 15 mm zone with 15 μg rifampicin disc, usually shows large zone with 1000 μg kanamycin disc, 6-25 mm zone with 1000 μg neomycin disc, usually inhibited by bile, indole and lipase positive, esculin negative; terminal pH glucose 6.0-6.9, propionic acid from lactate; oral; causes bacteraemia and septicemia, cervical fascial space infections, endocarditis, infections in abnormal host, 22% of anaerobic dental infections, chronic otitis externa; produces phospholipase A, lysophospholipase; treatment: metronidazole (100% susceptible), tetracycline, lincomycin; susceptible to ticarcillin (MIC ≤ 1 mg/L), ticarcillin-clavulanate (≤ 1 mg/L), clindamycin (100%)

F.necrophorum subspecies funduliforme: new subspecies

F.necrophorum subspecies necrophorum: new subspecies

F.nucleatum: variable length and width; inhibited by 0.1% deoxycholate, usually inhibited by bile, butyric acid from glucose or amino acids, does not produce gas, indole positive; esculin and lipase negative; susceptible to erythromycin, rifampicin, colistin, penicillin, kanamycin; resistant to vancomycin; lytic reaction on egg yolk agar; most commonly isolated *Fusobacterium* species; oral; causes endocarditis, infections in abnormal host, 40% of anaerobic head and neck infections, 32% of anaerobic CNS infections, necrotising pneumonia and pulmonary abscess (29% of transtracheal aspirates and pleural fluids growing anaerobes), 28% of anaerobic human bite infections, 22% of miscellaneous soft tissue infections above waist, 15% of anaerobic animal bite infections, 13% of anaerobic intraabdominal infections; adheres to epithelial cells, Gram positive and Gram negative bacteria, red blood cells; treatment: metronidazole (100% susceptible), tetracycline, lincomycin; also susceptible to ticarcillin (MIC ≤ 1 mg/L), ticarcillin-clavulanate (≤ 1 mg/L), clindamycin (100%)

F.nucleatum subspecies fusiforme: new subspecies

F.nucelatum subspecies nucleatum: new subspecies

F.nucleatum subspecies polymorphum: new subspecies

F.periodonticum: new species

F.russii: gas produced; indole, esculin, threonine and lactate negative

F.ulcerans: new species

F.varium: indole positive; esculin and lipase negative; propionic acid from threonine, butyric acid from glucose, not inhibited by 20% bile, weak or no action on carbohydrates; ≥ 20 mg zone of inhibition with 2U penicillin disc, small or no zone with 15 μg rifampicin disc or 60μg erythromycin disc; susceptible to chloramphenicol, metronidazole

Leptotrichia buccalis: obligately anaerobic Gram negative rods, nonsporeforming, peritrichous flagella or nonmotile, produces only lactic acid; normal flora of mouth, tooth surface; believed to play a role in causation of necrotising ulcerative gingivostomatitis, necrotising ulcerative pharyngitis and necrotising ulcer of the skin surface (tropical ulcer); causes bacteremia and septicemia in cancer patients, cat and dog bite infections; susceptible to β-lactams, clindamycin, tetracycline, metronidazole

Streptobacillus moniliformis: pleomorphic rods, frequently in wavy chains or tangled filaments with thickenings along the filaments, resulting in a 'string of pearls' or 'monilia-like' appearance; asporogenous; facultatively anaerobic; grows in serum broth producing discrete 'fluff ball-like' colonies; nonmotile; fastidious; no growth on MacConkey; usually requires a moist environment and blood, serum or ascitic fluid; indophenol oxidase and catalase not produced; ferments glucose (no gas) and maltose (weakly); negative test reactions for indole and nitrate; characteristic spontaneous appearance of defective cell walls; natural habitat nasopharynx of rats, mice and other rodents; cause of epizootics among animals; causes streptobacillosis; human infection following rat bite causes one form of rat-bite fever; human infection following consumption of contaminated milk referred to as haverhill fever; infection also follows drinking contaminated water; complications, usually in compromised patients, include endocarditis (rare), brain abscess, amnionitis, bronchitis, pneumonia and persistent septic arthritis; diagnosis: isolation in artificial medium, serology; treatment: penicillin, tetracycline, erythromycin

Phylum Proteobacteria

Class Alphaproteobacteria

Order Caulobacteriales

Family Caulobacteraceae

Brevundimonas diminuta: very tightly coiled monotrichous flagellum, with a wavelength that varies from 0.62-0.98μm, a distinctive characteristic of *B.diminuta* and *B.vesicularis* (wavelength of most polar monotrichous *Pseudomonas* ≈ 2 μm); colonies usually chalk-white in colour; indophenol oxidase produced; most carbohydrates not oxidised, although a few strains produce weak acid from glucose; acid produced from primary alcohols by all strains that utilise alcohols; pellicle forms in broth cultures; rarely reduces nitrate; esculin not hydrolysed; panthothenate, biotin, cyanocobalamin and cystine required as growth factors; isolated from streams, ditch waters, contaminated cell culture, respiratory equipment and various clinical specimens, such as blood, CSF and urine; clinical significance uncertain

B.vesicularis: very tightly coiled monotrichous flagellum, with a wavelength that varies from 0.62-0.98 μm—a distinctive characteristic of this species (and *B.diminuta*); indophenol oxidase produced; variable oxidation of glucose, xylose and maltose; nitrate usually not reduced; requires pantothenate, biotin and cyanocobalamin as growth factors; distinguished from closely related *B.diminuta* by esculin hydrolysis, production of an orange intracellular pigment (variable) and failure to produce a pellicle in broth culture; isolated from urinary bladder epithelium of a medicinal leech, whooping cough plate, tap water aerator, hospital sink, and human sources, such as cervical specimens, CSF, blood and urine; susceptible to doxycycline (MIC ≤ 0.03-0.25 mg/L)

Order Rhizobiales

Family Bartonellaceae

Bartonella: small, motile, fastidious, Gram negative bacilli; arthropod vectors, mammalian hosts (man, cattle, small rodents, coyotes, deer, cats)

B.bacilliformis: Gram negative bacilli, flagella; humans definitive reservoir host; causes bartonellosis (Oroya fever; invasion of vascular endothelial cells and haemolytic anaemia); carried in blood associated with erythrocytes; immunologically characterised by recurrent attacks of verruga peruana and selective suppression of resistance to *Salmonella*; diagnosis: stained smears of material from skin lesions, blood cultures; treatment: tetracycline

B.elizabethae: single report of endocarditis

B.henselae: small gram negative bacillus, often slightly curved; no flagella but produces twitching motion when suspended in saline; aerobic, highly fastidious, grows in presence of 5% CO_2 after 7 or more days; no acid from carbohydrates, catalase, oxidase, indole and urease negative, nitrates not reduced; causes bacillary angiomatosis, bacillary peliosis, cat scratch disease, hepatitis, prolonged or relapsing fever with persistent bacteraemia and constitutional symptoms; louse vector; reservoir man; diagnosis: Warthin-Starry stain and culture of biopsy, PCR; treatment: erythromycin, doxycycline, tetracycline, minocycline

B.quintana: no flagells; humans definitive reservoir host; causes trench fever (recurrent episodes of fever), bacillary angiomatosis, bacillary peliosis; treatment: erythromycin, doxycycline, tetracycline, minocycline, rifampicin, ciprofloxacin

B.rochalimae: multiple flagella; causes bacteremia, splenomegaly; treatment: levofloxacin

B.vinsoni subsp berkhoffii: single report of endocarditis

Family Bradyrhizobiaceae

Afipia felis: motile; no growth on MacConkey; oxidase and urease positive; NaCl, carbohydrate fermentation, citrate, indole, gelatine, esculin, H_2S, decarboxylases and cetrimide negative; 11-methyloctadec-12-enoic acid present

Family Brucellaceae

Brucella: Gram negative coccobacillus; asporogenous; nonmotile; obligately aerobic; slow growing and fastidious; most strains require complex media; growth improved by serum or blood, but not X or V factors; many strains require CO_2; growth on MacConkey strain variable; growth on agar plate after 18-24 h incubation scant and usually occurs only in areas of heavy inoculum; discrete colonies usually develop after further incubation; catalase, and usually indophenol oxidase, positive; nitrate reduced to gas by some species; indole not produced; does not liquify gelatine; urease positive (except *B.ovis*); criteria for identification of species and biovars: production of H_2S detected with lead acetate paper, requirement for CO_2, tolerance to dyes, urease activity and agglutination in monospecific sera; recognised major species *abortus, canis, melitensis* and *suis*; additional minor species *neotonae, ovis*; other strains not coinciding with descriptions of major or minor species; DNA hybridisation indicates genus consists of single species (*B.melitensis*); facultative intracellular parasite; transmitted to a wide range of animal species, including humans; pathogen of goats, cattle and pigs with secondary human infection; risk of laboratory infections as dangerous as with *Francisella tularensis*; causes brucellosis (> 100 cases/10 000/y in Longreach district), anterior uveitis, septic arthritis (in 9-37% of infections), bone marrow infection, endocarditis, acute epididymitis and epididymoorchitis (in 9% of infections), erythema nodosum, adult hepatitis, 2% of hepatic granuloma, lymph gland infection (in 50% of infections: most common physical finding in brucellosis), nonpyogenic meningitis (in < 5% of infections), osteomyelitis and osteochondritis, pneumonia, undulant fever; multiplies in macrophages; pathogenesis characterised by granuloma formation and delayed hypersensitivity; carried in blood associated with mononuclear cells; diagnosis: bone marrow culture, blood culture, direct immunofluorescence after incubation in nutrient broth, standard tube agglutination, dithiothreitol test (IgG), antihuman globulin test, complement fixation test (IgG), ELISA (IgG), lymphocyte proliferation assay; treatment: doxycycline, rifampicin (MIC 0.06-1 mg/L), streptomycin, cotrimoxazole (≤ 0.25-1 mg/L), oxytetracycline, gentamicin, ampicillin, chloramphenicol, tetracycline (≤ 0.13-0.25 mg/L); also susceptible to ciprofloxacin (0.5-1 mg/L)

B.abortus: usually susceptible to 1:100 000 thionine, usually resistant to 1:50 000 basic fuchsin, 1:400 crystal violet and 1: 8000 pyronine; CO_2 required on primary isolation (strain variable); indophenol oxidase produced; oxidises xylose and usually glucose; no gas from nitrate; slow hydrolysis of urea (1-2 h, rarely 24 h); H_2S variable; lysed by phage TB5; L-glutamic acid and D-ribose positive; DL-ornithine and L-lysine negative; cell wall substance resists killing by phagocytes; inhibits phagocytic oxidative burst and microbicidal activity by resistance to oxidative attack; natural hosts cattle and other bovidae, but also horses, camels, sheep, deer, dogs and humans; isolated from human blood, bone marrow and abscess; causes brucellosis (abortus fever), bursitis in humans, abortion in animals

B.canis: CO_2 not required; oxidises xylose and glucose; indophenol oxidase production variable; variable gas from nitrate; urease activity within 30 min; H_2S not produced; usually susceptible to basic fuchsin and resistant to thionine dyes; biochemically similar to *B.suis*; natural host dogs; causes orchitis and prostatitis in males and placentitis and abortion in females; isolated from human blood; infection occasionally transmitted to humans (brucellosis)

B.melitensis: resistant to 1:100 000 thionine, 1:50 000 basic fuchsin, 1:400 crystal violet and 1:8000 pyronine; CO_2 not required; hydrolysis of urea immediate or delayed (2 h, rarely 24 h); L-glutamic acid positive; H_2S, DL-ornithine, L-lysine and D-ribose negative; not lysed by phage; oxidises xylose and usually glucose; indophenol oxidase produced; no gas from nitrate; natural hosts usually sheep and goats, but also cattle, pigs and humans; isolated from human blood, bone marrow, bile and spleen; causes abortion in animals, brucellosis (Bruce septicemia, country fever of Constantinople, Cyprus fever, febris melitensis, Gibraltar fever, goat-milk fever, Malta fever, Mediterranean fever, melitensis septicemia, mountain fever, Neapolitan fever, new fever (Crete), Rio Grande fever, Rock fever (Gibraltar)), brain and epidural abscess (rare); treatment: cotrimoxazole; also susceptible to ciprofloxacin (MIC 0.5-0.8 mg/L), ofloxacin (0.8 mg/L)

B.neotonae: CO_2 not required; positive urease in 15 min; H_2S positive; no growth on media containing 1:50 000 thionine or fuchsin

B.ovis: CO_2 required; positive urease in $\geq$ 7 d; H_2S negative; resistant to 1:50 000 thionine, most strains susceptible to 1:50 000 fuchsin

B.suis: usually resistant to 1:100 000 thionine, usually susceptible to 1:50 000 basic fuchsin, 1:400 crystal violet and 1:8000 pyronine; CO_2 not required; rapid hydrolysis of urea (within 30 min); H_2S, L-glutamic acid and D-ribose variable; DL-ornithine and L-lysine positive; not lysed by phage; oxidises xylose and glucose; indophenol oxidase produced; gas from nitrate variable; natural hosts usually pigs, horses, rodents, reindeer, but also dogs and humans; isolated from human blood, bone marrow, lung tissue and spleen; causes brucellosis in humans, abortion in animals

Ochrobactrum anthropi: rods motile by peritrichous flagella; only 1 or 2 polar or lateral flagella found in some isolates; obligately aerobic; asporogenous; indophenol oxidase and catalase produced; oxidises xylose as well as other carbohydrates, excluding lactose; reduces nitrate to gas; hydrolyses urea (rapid); phenylalanine deaminated; indole not produced; distinguished from phenotypically similar *Agrobacterium* strains by failure to oxidise lactose and negative test for ONPG; natural habitat water; recovered from human wound, urine, sputum and blood; rarely clinically significant; cause of pancreatic abscess, septicemia in an immunocompromised host (catheter related) and puncture wound osteochondritis; treatment: cotrimoxazole

Family Methylobacteriaceae

Methylobacterium: pleomorphic, branched, vacuolated rods; cells contain large sudanophilic enclosures and volutin granules; tendency to resist Gram decolourisation; asporogenous; usually motile with a single polar flagellum; obligately aerobic; facultative methanol oxidiser; produces a pink to red pigment; grows poorly on media used for pseudomonads; growth occurs best on Saboraud's agar, buffered charcoal yeast extract agar or Middlbebrook and Cohn 7H11 agar; growth may occur better at 30°C than 35°C; indophenol oxidase, catalase, urease and amylase reactions produced; nitrate reduction variable (no gas); indole not produced; isolated from a wide range of habitats, such as soil, water (river, bay, lake, tap), air, rice grain, sewage, semen of cows, and hospital environment, but primarily from leaf surfaces and leaf nodules of plants (perennial rye grass, tobacco, soybean); occasionally isolated from clinical specimens, including blood, endocervix, throat, ulcer, ascitic fluid, skin lesion and bronchial washing; rarely clinically significant; source of nosocomial infection in a bone marrow transplant unit, bacteremia in a patient with metastatic adenocarcinoma of the lung and probably associated with chronic skin ulcer infection

M.extorquens: causes bacteremia and septicemia (catheter related); treatment: gentamicin, amoxycillin-clavulanate, piperacillin, cotrimoxazole, rifampicin, fluoroquinolone

Family Rhizobiaceae

Rhizobiaceae

Agrobacterium: causes peritonitis in continuous ambulatory peritoneal dialysis

A.tumefaciens: rods motile by 1-6 peritrichous flagella; only 1 or 2 lateral flagella in some isolates; obligately aerobic; asporogenous; positive test reactions for indophenol oxidase, catalase, phenylalanine deaminase and hydrolysis of urea (rapid), esculin and ONPG; nitrate usually reduced (occasionally with gas); oxidises glucose, xylose, lactose, sucrose, maltose and mannitol; indole not produced; oxidative acidity from lactose and the production of 3-ketolactose (biovar 1, not biovar 2) separates biovar 1 of this species from phenotypically similar strains of *Achromobacter* CDC group Vd; some biovar 2 strains fail to grow at 35°C; primarily known as a phytopathogen; isolated from moist soil and from around roots of plants as well as from galls and tumours of diseased plants; isolated from human sputum, wound, blood, bronchial washing, tracheal aspirate, eye, urine, synovial fluid, ear, vagina, colon and endometrium; rarely clinically significant, usually contaminant; cause of bacteraemia and septicemia (intravascular catheter, artificial ventilation, adenocarcinoma), prosthetic valve endocarditis, urinary tract infection in a patient with nonfunctioning kidney, peritonitis in continuous ambulatory peritoneal dialysis; treatment: gentamicin, amoxycillin-clavulanate, piperacillin, cotrimoxazole, rifampicin, fluoroquinolone; also susceptible to ticarcillin, cefoxitin, cefuroxime, ceftriaxone, cefotaxime; resistant to aztreonam, tobramycin

Order Rhodobacterales

Family Rhodobacteraceae

***Paracoccus yeei*:** coccobacilli, usually vacuolated; asporogenous; obligately aerobic; oxidative in glucose, xylose and lactose and usually fructose and mannitol but not sucrose; nonmotile; indophenol oxidase and catalase produced; nitrate and urea reactions strain variable; indole not produced; difficult to distinguish from animal strains of *Psychrobacter* that oxidise carbohydrates and grow at 35°C; some *Paracoccus yeei* strains, but not *Psychrobacter* strains, grow at 42°C and produce acid from mannitol; isolated from horse blood, hemodialysis water and human clinical sources, including wound, eye, vagina, blood and others; clinical significance unknown

Order Rhodospirillales

Family Acetobacteraceae

***Acetobacter*:** rare opportunistic invader

Roseomonas: Gram negative; non-fermentative; pink-pigmented, slimy colonies; waterborne; includes CDC Pink Coccoid Groups I-IV; rare opportunistic human infections

Family Rhodospirillaceae: purple nonsulfur bacteria

Inquilinus limosus: isolated from cystic fibrosis sputum; pathogenicity uncertain

Order Rickettsiales: not deficient in basic energy metabolic functions; rigid cell envelope; no growth on cell-free media (few exceptions); cell wall or cell wall peptidoglycan present; do not require sterols; usually arthropod parasites

Family Anaplasmataceae

Anaplasma phagocytophila: causes granulocytic ehrliciosis

Ehrlichia: causes ehrlichiosis, ? mucocutaneous lymph node syndrome; growth stimulated by excess iron; diagnosis: serology, immunohistologic examination of acute phase bone marrow and liver biopsy; treatment: doxycycline, tetracycline

E.canis: causes monocytic ehrlichiosis

E.chaffeensis: causes human monocytic ehrlichiosis

E.ewingii: causes human and canine granulocytic ehrlichiosis

E.sennetsu: causes monocytic ehrlichiosis, Hyuga fever; treatment: doxycycline, tetracycline

Family Rickettsiaceae: only group of bacteria that are obligate intracellular parasites transmitted by arthropods

Tribe Rickettsieae

Orientia tsutsugamushi: causes scrub typhus (tsutsugamushi disease, Japanese river fever, Kadani fever, rural typhus; fever, eschar, rash); Japan, Korea, China, Philippines, SE Asia, Indian subcontinent, Indonesia, N Australia, Pacific Islands; vector trombiculid mites; reservoir native rodents, bandicoots, ? birds; typhus, RMSF, OX19 and OX2 negative; OXK^{+++}; escapes from phagosome; treatment: tetracycline, doxycycline, chloramphenicol

Rickettsia: no growth in nonliving media; causes rickettsioses, scrub typhus, spotted fevers, typhus, encephalitis, localised skin lesions, hemorrhagic rash, macular rash, maculopapular rash; transmitted by infestation with infected arthropod; enters across skin epithelial surface and subsequently spreads through body; carried in blood free in plasma; multiplies inside tissue cells; primary immune defence prevention of entry into cells by coating microbial surface with specific antibody (IgG, IgA, IgM), killing of infected cell also important; treatment: tetracycline, chloramphenicol, doxycycline, cotrimoxazole

Spotted Fever Group

R.akari: causes rickettsialpox; urban localities in NE USA, former Soviet Union, Korea, Southern Africa, Mediterranean; mite vector; house mice, rat reservoir; typhus^{+++}, RMSF^{+++}; OX19, OX2 and OXK negative; treatment: tetracycline, doxycycline

R.australis: causes North Queensland tick typhus; Australia; vector tick; reservoir ? rat, ? marsupial; OX19^{+}, OX2^{+}; OXK negative; treatment: tetracycline, doxycycline

R.conorii: causes Boutonneuse (Marseilles, Mediterranean) fever (Mediterranean, Caspian and Black Sea littoral, Middle East), Indian tick typhus (India), Kenya tick typhus (E Africa), adult hepatitis, nonpurulent conjunctivitis (in 32% of cases); vector tick (*Rhicephalus sanguineus*); reservoir dog, rodents; OX19^{+}, OX2^{+}; OXK negative; diagnosis: microimmunofluorescence, latex agglutination of serum, immunofluorescence of skin biopsy, Western blot, isolation from blood culture with shell vial cell culture; treatment: tetracycline, doxycycline

R.honei: causes Flinders Island spotted fever; tick (*Ixodes holocyclus* and *Ixodes tasmani*) vector

'R.pijperi': causes tick bite fever (hamorrhagic fever); S Africa; reservoir ? rodents; OX19^{+}, OX2^{+}; OXK negative; treatment: tetracycline, doxycycline

R.rickettsii: Western hemisphere; causes Rocky Mountain spotted fever (N America), Sao Paulo typhus (Brazil), Tolia fever (Colombia), adult hepatitis, anterior uveitis, myocarditis and pericarditis (in 5% of infections), nonpurulent conjunctivitis (in 30% of infections), hemorrhagic fever; ticks vector; rabbits, small rodents, dog, opossum reservoir; typhus$^{\pm}$, RMSF^{+++}, OX19^{+++}, OX2^{+++}; multiplies in macrophages; treatment: tetracycline, chloramphenicol, doxycycline; also susceptible to erythromycin, rifampicin, streptomycin, thiomycetin

R.siberica: causes Siberian tick typhus; Central Asia; tick vector; rodents, dog reservoir; typhus$^{\pm}$, RMSF^{+++}, OX19^{+++}, OX2^{+++}; OXK negative; treatment: tetracycline, doxycycline

Typhus Group

R.canadensis: susceptible to tetracycline, chloramphenicol

R.prowazekii: causes epidemic (classic, European, louseborne) typhus (fever, encephalitis, haemorrhagic rash); worldwide (Europe, Asia, America); human louse (*Pediculus humanus corporis*) vector (infected louse faeces rubbed into broken skin or as aerosol to mucous membranes); reservoir man, squirrel; typhus^{+++}, RMSF$^{\pm}$, OX19^{++++}, OX2^{+}; OXK negative; multiplies in macrophages; transmitted in blood; persists in lymph node (? infectious, shed to exterior), activation months or years after primary attack giving Brill-Zinsser disease (typhus^{+++}, RMSF$^{\pm}$, OX19$^{\pm}$; OX2 negative); 1000 genes; treatment: tetracycline, chloramphenicol, doxycycline

R.typhi: causes murine (endemic, fleaborne) typhus; scattered pockets worldwide; flea (*Xanopsylla cheopsis*) and rat louse vectors; wild rats and field mice reservoir; typhus^{+++}, RMSF$^{\pm}$, OX19^{++++}, OX2^{+}; OXK negative; treatment: tetracycline, chloramphenicol, erythromycin, rifampicin, streptomycin

Order Sphingomonodales

Family Sphingomonadaceae

Pseudomonas paucimobilis: colonies develop an intracellular, nondiffusible, yellow pigment; occasionally, only a few cells in a population motile (polar monotrichous); indophenol oxidase usually produced; oxidative in a wide variety of carbohydrates, but not mannitol; esculin and ONPG hydrolysed; negative test reactions for urease, nitrate, dihydrolases and decarboxylases; lack of urease distinguishes non-motile strains from phenotypically, but not genotypically, similar *Sphingobacterium multivorum*; isolated from water, hospital environment, including distilled water, respirator, humidifier and dialysis fluid, and from human vaginal and cervical swabs, blood, CSF, urine, wound, splenic abscess, post-operative and post-traumatic wound infections and septicemia; cause of a community-acquired septicemia in a patient on chronic corticosteroid therapy; causes acute skin ulcers; treatment: ciprofloxacin (MIC $<$ 0.5 mg/L); also susceptible to minocycline (MIC $\leq$ 0.03-0.13 mg/L), norfloxacin ($<$ 0.5 mg/L)

Zymomonas: causes bacteremia and septicemia (uncommon in neutropenics)

Class Betaproteobacteria

Order Burkholderiales

Family Alcaligenaceae

Achromobacter: glucose negative; oxidase and motility positive; normal flora of large intestine, lower ileum; causes endophthalmitis (postoperative), postoperative and posttraumatic wound infectious complications

A.piechaudii: nonoxidiser; reduces nitrate (no gas), but not nitrite; grows on cetrimide; utilises gluconate; no growth at 42°C; colonies circular, smooth, entire; isolated from soil and human pharyngeal swab, nose and blood; clinical significance not determined

Alcaligenes denitrificans: motile; nonoxidiser; reduces both nitrate and nitrite to gas; colonies low convex, glistening, entire; isolated from soil, water, hospital environment and a variety of clinical specimens, such as faeces, urine, blood, pleural fluid, ear discharge, prostatic secretion and throat swab; clinical significance unknown

A.xylosoxidans xylosoxidans: oxidises xylose; variable weak oxidation of monosaccharides; reduces both nitrate and nitrite with variable gas; grows on cetrimide; colonies convex, smooth, glistening, entire; negative tests for urease and phenylalanine deaminase distinguish this species from phenotypically similar *Achromobacter* CDC group Vd; natural habitat water; isolated from disinfectant solution, saline, deionised water, swimming pool, hospital sink and a wide range of human clinical material, including blood, sputum, wound, ear discharge, CSF, pleural fluid, tracheal aspirate, cerebral tissue, urine and faeces; infrequent but potentially serious nosocomial organism with a predilection for compromised patients; cause of catheter related endocarditis in bone marrow transplant recipients, postoperative and posttraumatic wound infections, pneumonia, urinary tract infection, neonatal meningitis, peritonitis, biliary tract sepsis, both nosocomial and community-acquired chronic otitis media, chronic pulmonary infection in cystic fibrosis, bacteraemia and septicemia (rare catheter related and gastrointestinal, especially in cancer patients); treatment: cotrimoxazole, ciprofloxacin

Alcaligenes: rods or coccal rods; motile with 1-8, occasionally up to 12, peritrichous flagella; asporogenous; good growth on MacConkey; simple nitrogenous growth requirements; growth on SS and at 42°C variable; colonies nonpigmented; obligately aerobic (some strains utilise nitrite instead of oxygen as final electron acceptor); catalase produced; nitrate reduction variable; indole not produced; usually negative tests for arginine dihydrolase, lysine decarboxylase, ornithine decarboxylase, phenylalanine deaminase, amylase, DNAse, gelatinase; oxidase positive; oxidative (1 subspecies only) or nonreactive; occurs in water and soil; causes bacteraemia and septicemia (uncommon in neutropenics), swimmer's ear, other suppurative conditions; growth stimulated by excess iron; 100% susceptible to imipenem; resistant to ciprofloxacin (except *A.xylosoxidans*), ofloxacin, pefloxacin

A.faecalis: nonoxidiser; colonies large, umbonate with a spreading periphery, and granular; reduces nitrite with gas, but not nitrate; grows on cetrimide; hydrolyses acetamide; causes green discolouration of blood on blood agar media; produces a distinctive fruity odour; motile; normal flora of large intestine, ileum, cervix (3%); occurs in soil and water; isolated from nematodes, insects and numerous clinical specimens, such as faeces, urine, blood, sputum, wound and pleural fluid; rarely

clinically significant; causes bacteraemia and septicemia, gastroenteritis (rare), nosocomial urinary tract infection, pneumonia (occasional), infections in abnormal host

***A.faecalis* types I and II:** nonoxidiser; nitrite not reduced; type I strains reduce nitrate (no gas) and produce small, low convex, glistening colonies with a entire edge; type II strains fail to reduce nitrate and produce larger, umbonate, granular colonies with a spreading periphery; carbon substrate utilisation further distinguishes 2 types; isolated from soil, water and a number of human clinical specimens, primarily ear discharge, blood and sputum; rarely clinically significant; cause of endocarditis and septicemia

Bordetella: minute Gram negative bacillus or coccobacillus; asporogenous; nonmotile or motile with usually 1-8 peritrichous flagella; obligately aerobic; some species fastidious and require modified media for isolation and primary growth; nicotinic acid, cystine and methionine required by some strains for growth; growth on MacConkey poor or negative; no acid produced from carbohydrates; catalase positive (except for some *B.pertussis* strains), oxidase positive (except for *B.parapertussis)*; mammalian parasite; all species can produce infections of respiratory tract; susceptible to ciprofloxacin (MIC 0.5 mg/L)

B.avium: rods motile by peritrichous flagella; capsulated; somewhat fastidious; grows on cetrimide, MacConkey and SS agars; hydrolyses acetamide; urease and phenylalanine deaminase not produced; nitrate not reduced; 2 morphovars: type I colonies small, compact, pearl-like, entire edges, glistening surface; type II colonies larger, circular, convex, entire edges, smooth surface; probably misidentified as *Alcaligenes faecalis*; differentiated from latter on basis of requirement for undetermined amino acids and vitamins as growth factors in a mineral base medium; parasite of respiratory epithelium of birds; cause of respiratory disease in birds (turkeys); susceptible to penicillin, polymyxin and most other antimicrobials

B.brochiseptica: rods, motile by peritrichous flagella; nonfastidous; grows well on blood agar as hazily haemolytic colonies; utilises acetate in a mineral base medium without growth factors; grows on MacConkey agar; nitrate reduced (no gas); rapid urea hydrolysis distinguishes this species from similar strains of *Alcaligenes faecalis*; reduction of nitrate (no gas), growth on SS agar and failure to utilise gluconate distinguishes this species from similar group IVc-2 strains; commensal in respiratory tract of animals; humans serve as an accidental host; most infections occur in patients with close contact with animals, including dogs, cats, rabbits, turkeys, foxes, skunks; cause of human respiratory (acute tracheitis, bronchitis, tracheobronchitis, bronchopneumonia, pneumonia) and non-respiratory (endocarditis, posttraumatic meningitis, peritonitis) infections; susceptible to doxycycline (MIC 0.06-0.25 mg/L), imipenem (100%)

B.parapertussis: minute coccobacillus; nonmotile; requires complex growth factors; usually produces β-hemolysis; growth more rapid on Bordet-Gengou medium than with *B.pertussis*; growth on peptone agar accompanied by a brown discolouration of medium; nitrate not reduced; distinguished from *B.pertussis* by growth on MacConkey agar, urease activity (24 h) and negative indophenol oxidase reaction; found only in respiratory tract of humans; multiplies among epithelial cilia of respiratory tract; causes human infections similar to whooping cough; susceptible to ciprofloxacin (MIC 0.06 mg/L), ofloxacin (0.5 mg/L)

B.pertussis: minute coccobacillus; nonmotile; more fastidious than other *Bordetella*; requires complex growth factors; no growth on usual laboratory media; Bordet-Gengou medium or charcoal agar preferred for primary isolation; usually produces β-like hemolysis, but not as distinct as that produced by *B.parapertussis*; nitrate not reduced; distinguished from *B.parapertussis* by negative reactions for growth on MacConkey agar and urea hydrolysis and positive reactions for indophenol oxidase; found only in respiratory tract of humans; specialised human respiratory parasite; attaches to respiratory epithelium; multiplies among epithelial cilia of respiratory tract; infection generally confined to epithelial surface of respiratory tract; inhibits phagocyte function by bacterial adenylate cyclase; toxin causes ciliary damage; cell wall increases sensitivity to histamine, produces lymphocytosis, causes fasting hypoglycaemia and prevents hyperglycaemia; phase I and phase IV cultures are differentiated by vaccine effectiveness against infection, nutritional requirements and antigenic makeup; causes pertussis (whooping cough), catarrh; treatment: erythromycin, cotrimoxazole; also susceptible to rosoxacin (MIC 0.025 mg/L), ciprofloxacin (0.2 mg/L), ofloxacin (0.12-0.25 mg/L), norfloxacin (0.25 mg/L), enoxacin (0.15-0.5 mg/L)

Oligella: small Gram negative rods often occurring in pairs; asporogenous; obligately aerobic; no acid production from carbohydrates; slowly developing colonies on blood agar similar to colonies of *Moraxella*; nonpigmented; indophenol oxidase, catalase and phenylalanine deaminase, but not indole, produced; utilises acetate in a mineral base medium; usually isolated from genitourinary tract of humans

O.ureolytica: nonmotile or motile with peritrichous flagella, often with 1 polar, and only a few lateral, flagella; most strains reduce both nitrate and nitrite (with gas); produces urease (rapid); no growth at 42°C; saprophytes from human urine; susceptible to netilmicin (MIC ≤ 0.03-0.25 mg/L); resistant to penicillin

O.urethralis: nonmotile; nitrate not reduced; nitrite reduction to gas strain variable; urease not produced; grows at 42°C; 1/3 catalase positive; growth on MacConkey; gelatine negative; natural habitat the human genitourinary tract; isolated as a saprophyte from urine and from the female genital tract, also wound, ear, nose, throat, blood; pathogenicity unknown; susceptible to penicillin

Taylorella equigenitalis: glucose negative

Family Burkholderiaceae

Burkholderia cepacia: some strains produce a green-yellow, water-soluble, nonfluorescent phenazine pigment; pigment occurs in bacterial cell and usually diffuses into surrounding agar medium; many strains non-pigmented; motile with a polar tuft (3-many) of flagella; oxidative activity from a wide range of carbohydrates, including glucose, lactose, maltose and mannitol; most strains hydrolyse ONPG and produce decarboxylases of lysine and ornithine; nitrate not reduced to gas; occasionally, a very weak or negative indophenol oxidase reaction; not susceptible to polymyxin or colistin; isolated from rotten onions, as a phytopathogen, from soil from a variety of geographical regions, hospital environment, and various clinical specimens, including urine, blood, CSF, bronchial washing, sputum, abscess and wound; part of increased flora during myelosuppressive therapy; an opportunistic organism associated with various types of human infections of community-acquired and nosocomial origins, including septicemia, meningitis, endocarditis, pneumonia, chronic pulmonary infection in cystic fibrosis, post-operation wound infection, urinary tract infection, septic arthritis, chronic granulomatous disease, cervical osteomyelitis, endophthalmitis, endotoxic reactions associated with reuse of cardiac catheters, nosocomial infection from cryoprecipitate contaminated in water bath, pseudobacteremia due to contaminated povidone iodine solution; variably susceptible to imipenem, meropenem; resistant to gentamicin, amikacin, ampicillin, amoxycillin, amoxycillin-clavulanate, cephalothin, cefaclor, cefixime, cefuroxime, cephalexin, ciprofloxacin and many others

B.gladioli: motile with a single polar flagellum; produces acid from glucose, xylose and mannitol; ONPG positive; resistant to polymyxin; negative test reactions for indophenol oxidase, oxidation of lactose, sucrose and maltose and decarboxylases for lysine and ornithine and a positive test reaction for urease distinguishes from closely related *Burkholderia cepacia*; isolated from decayed onions and respiratory specimens of patients with cystic fibrosis; otherwise, rarely recovered from human clinical specimens

B.mallei: fluorescent pigment absent; colonies smooth and range from white to cream in colour; grows slowly compared with *P.aeruginosa* or *Burkholderia pseudomallei*; no growth on MacConkey; non-motile; slow and very weak or negative indophenol oxidase reaction; slowly oxidative in glucose and a wide range of other carbohydrates, including cellobiose and maltose, but not xylose or maltose; arginine dihydrolase produced; not susceptible to polymyxin; negative test reactions for nitrogen gas, gelatinase, Simmon's citrate, lysine decarboxylase and growth at 42°C; causes glanders (farcy) of equines (transmitted from equine hosts to humans by direct contact and transmitted from person to person; quite rare); only highly adapted parasite of animals in the genus; diagnosis: Gram stain and culture of swab of discharge from necrotic foci or skin or from enlarged lymph nodes, blood, sputum, nasopharyngeal discharge, complement fixation test, agglutinations; treatment: sulphonamides, cotrimoxazole

B.pseudomallei: colonies vary from mucoid and smooth to rough and wrinkled in texture and from bright orange to cream colour; fluorescent pigment absent; characteristic musty, earthy odour; Gram negative rods, bipolar staining (safety pin appearance); motile with a polar tuft of 3 or more flagella; growth at 42°C, no growth at 4°C; nitrate reduced to nitrite and nitrogen gas; grows anaerobically in a nitrate-containing medium accompanied by gas production; oxidative in glucose, lactose, maltose, sucrose, cellibiose, starch and a wide variety of other carbohydrates; slow and very weak indophenol oxidase reaction; catalase positive; arginine dihydrolase produced; proteolytic; not susceptible to polymyxin, colistin or aminoglycosides; Simmon's citrate positive, lysine decarboxylase negative, methionine not required; alkaline phosphatase heat resistant; free-living organism isolated from soil or water in restricted geographical regions (endemic between 20°N and 20°S latitudes); causes melioidosis (an endemic glanders-like disease of humans and animals in SE Asia and Northern Australia; rarely occurs in Western hemisphere), bacteraemia and septicemia (common in S E Asia in rice farmers or their families; associated with diabetes and renal failure; 85-95% mortality), hepatic abscess, adult hepatitis, hepatic granuloma, parotitis and sialadenitis, pneumonitis; diagnosis: culture of pus swab from ulcers and abscesses, sputum, urine, blood, indirect haemagglutination antibody titre, enzyme immunoassay IgG and IgM, immunofluorescence IgG and IgM; susceptible to trimethoprim, cotrimoxazole, doxycycline, ceftazidime, meropenem (MIC 0.78 mg/L), chloramphenicol, tetracycline, minocycline, amoxycillin-clavulanate, imipenem, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate; resistant to ampicillin

***Cupriavidus pauculus*:** rods motile by peritrichous flagella; asporogenous; obligately aerobic; indophenol oxidase and catalase produced; rapid urea hydrolysis (not as rapid as *Bordetella bronchiseptica*); no acid produced from carbohydrates; indole not formed; negative reactions for nitrate reduction and growth on SS agar differentiate from phenotypically similar strains of *Bordetella bronchiseptica*; environmental isolates, primarily from water; isolated from human blood, eye, sputum, urine, throat and peritoneal fluid; clinical significance probably low; cause of nosocomial septicemia in a patient with peripheral vascular disease and in a patient with plasma cell leukemia; susceptible to doxycycline (MIC 0.13-0.5 mg/L)

Pandoraea: isolated from cystic fibrosis sputum but pathogenic role unknown

Ralstonia: isolated from cystic fibrosis sputum but pathogenic role unknown

R.pickettii: growth of nonpigmented colonies on blood agar and other media characteristically slow; motile with a polar flagellum; indophenol oxidase produced; development of oxidative activity in O-F media and reduction of nitrate to gas characteristically slow, usually requiring 48 h of incubation to detect; urease produced; dihydrolase and decarboxylases not produced; not susceptible to polymyxin; alkali produced from malonate; mannitol, sucrose and ethanol not oxidised; several biovars differentiated by acidification of specific carbohydrates; isolated from environmental sources, such as water from an

artificial kidney machine, chlorhexidine solution, autoclave-cooling water, intravenous fluid, umbilical catheter tip, i.v. catheter, respiratory therapy saline solution, paper mill effluent and teething ring; isolated from human sources, including urine, nasopharynx, abscess, wound, blood and CSF; part of increased flora during myelosuppressive chemotherapy; primarily opportunistic; associated with a case of acute, non-fatal meningitis, infections of urinary and respiratory tracts and a number of cases of septicemia

Family Comamonadaceae

Acidovorax delafieldii: motile with a polar flagellum; indophenol oxidase produced; oxidative in glucose, xylose and mannitol, but not lactose, sucrose or maltose; produces positive test reactions for nitrate reduction (no gas), arginine dihydrolase, urease, DNAse and gelatinase; isolated from soil by enrichment procedures, pus from cement in femur, joint aspiration and trachea; no information concerning clinical significance

Comamonas: curved or straight rods; asporogenous; motile by means of a polar tuft of flagella with a mean wavelength of 3.1 μm, a distinctive characteristic; number of flagella at one or both poles varies from 1 to 6; obligately aerobic; indophenol oxidase and catalase produced; nitrate reduced (no gas); alkali produced in O-F carbohydrates except for weak acidification of fructose and mannitol by *C.acidovorans*; indole not produced; some strains require growth factors; growth not pigmented; soil and water saprophytes

C.terrigena: nonoxidative; differentiated from *C.testosteroni* in requiring growth factors (methionine and nicotinamide) in a mineral base medium for growth; utilises β-alanine, not histidine and phenylalanine; isolated from soil, water, hospital environment and human blood and faeces; clinical significance unknown

C.testosteroni: nonoxidative; distinguished from *C.terrigena* in having no growth factor requirements and by utilisation of histidine and phenylalanine, but not β-alanine, as sole source of carbon; isolated from soil, water, hospital environment and human blood, sputum and urine; rarely clinically significant

Delftia acidovorans: no growth at 42°C; oxidation of fructose and mannitol and production of anthranilic acid and kyneurenine in tryptone broth, which causes Kovacs reagent to turn orange, distinguishes this species from *C.terrigena* and *C.testosteroni*; isolated from soil, water, rat kidney, hospital environment and human urine, blood, sputum, eye, tracheal washing, suprapubic tap, pleural fluid, abdominal drainage and wound; rarely aetiologically significant; susceptible to oxolinic acid (MIC $\leq$ 0.25 mg/L), meropenem (0.25 mg/L), cefoxitin (0.5 mg/L), moxalactam (0.5 mg/L), ceftriaxone (0.5 mg/L), cefixime (0.5 mg/L), enoxacin (1 mg/L)

Unclassified Comamonadaceae

CDC Group NO-1: similar to asaccharolytic strains of *Acinetobacter* but different cellular morphology and cellular fatty acid profile; isolated from animal bites (77% dog, 18% cat, 5% unknown); susceptible to aminoglycosides, β-lactams, tetracycline, quinolones and sulphonamides

Order Neisseriales

Family Neisseriaceae

Chromobacterium violaceum: Gram negative rods motile by means of both a single polar flagellum and usually 1-4 lateral flagella; asporogenous; facultatively anaerobic; produces butyrous, violet colonies (nonpigmented colonies frequently produced); nonfastidious; grows on most ordinary media, including MacConkey and SS; attack on glucose and, rarely, sucrose usually fermentative, sometimes oxidative; nitrate and nitrite reduced (often with gas); oxidase positive; catalase and arginine dihydrolase produced; negative test reactions for lysine decarboxylase, ornithine decarboxylase and indole; common occurrence in soil and water in tropical regions (between 35°N and 35°S); isolated from human blood, wound, skin lesion, urine and ear; occasionally causes bacteraemia and septicemia (associated with abscesses in multiple organs), hepatic abscess, local pyogenic skin abscess, generalised fine rash, maculopapular rash, acute skin ulcers (in 11% of infections), local and generalised sepsis, pneumonia, pulmonary abscess, infections in abnormal host; high mortality in humans and domestic animals; treatment: chloramphenicol, tetracycline, gentamicin

Eikenella corrodens: slender straight rods or small Gram negative coccobacilli with regular morphology, nonbranching, nonencapsulated, occasionally filamentous; asporogenous; nonmotile; facultatively anaerobic; fastidious; growth enhanced by CO_2 and X factor (required aerobically, not anaerobically); variable slightly yellow pigment; usually pitting or corroding of colonies, with spreading edges, on blood agar; no growth on MacConkey; distinctive odour (bleach-like); no acid formed from carbohydrates; catalase not produced; positive test reactions for oxidase, nitrate (no gas), lysine decarboxylase and ornithine decarboxylase; negative test reactions for indole and urease; natural habitat normal adult human mouth and intestine; isolated from human wound, abscess, peritoneal fluid, blood, pleural fluid, sinus, pus, eye and bronchi; opportunistic pathogen; rarely sole isolate to initiate infection in host with normal immune status; in immunocompromsied host, usually sole isolate; causes deep abscesses (usually in sites where there has been mucous membrane flora contamination), infections in abnormal host, bacteraemia and septicemia following dental extraction, cervical fascial space infections, clenched fist injury and human bite infections, dental infections, cutaneous, wound and burn infections, other suppurative lesions, local and generalised sepsis, persisting empyema (rare), pneumonia, paronychia, abdominal abscess, pancreatic abscess, meningitis, osteomyelitis and osteochondritis (in 50% of infections related to human bite or fist fight injuries), septic arthritis (in 50% of infections relating to human bites or fist fight injuries), endocarditis; treatment: cefotaxime, ceftriaxone, amoxycillin-

clavulanate (always susceptible) chloramphenicol (generally susceptible), ampicillin (generally susceptible); also always susceptible to quinolones, generally susceptible to penicillin, tetracycline; always resistant to clindamycin, methicillin, flucloxacillin, metronidazole, most resistant to aminoglycosides

Kingella: plump rods or coccobacilli occurring in pairs or short chains; tendency to retain crystal violet of Gram stain; asporogenous; nonmotile; facultatively anaerobic; fastidious; little or no growth in unsupplemented peptone media; spreading and corroding or smooth and convex colony types on blood agar; indophenol oxidase, but not catalase, produced; urease not formed; glucose and a limited number of other carbohydrates fermented with acid production (no gas; delayed); growth on MacConkey scant or negative; distinguished from *Moraxella* by β-hemolytic and catalase negative; occurs in human mucous membranes of upper respiratory tract; susceptible to penicillin and most other antimicrobials

K.denitrificans: ferments glucose but not maltose or sucrose; usually reduces nitrate and nitrite (with gas); no growth on MacConkey but grows on Thayer-Martin selective agar; may pit agar surface; indole not produced; natural habitat the mucous membranes of the respiratory tract of humans; also isolated from human urogenital tract, mandibular abscess and blood; pathogenicity uncertain

K.kingae: ferments glucose and maltose but not sucrose; growth on MacConkey variable; usually β-haemolytic; negative test reactions for indole and usually both nitrate and nitrite reduction; normal flora of nasopharynx; isolated from human blood, bone, joint fluid, pustule, wound and urine; causes septic arthritis (mainly infants and young children), endocarditis in children (especially prosthetic valve patients), intervertebral disc infection in children, osteomyelitis and osteochondiritis (mainly infants and young children), acute meningitis in sickle cell anaemia, bacteraemia and septicemia in alcoholic liver disease and in children; treatment: penicillin

Neisseria: Gram negative aerobic (but strains of some species grow weakly under anaerobic conditions) cocci, single, but more often in pairs with adjacent sides flattened, or distinct short rods arranged as diplobacilli and in short chains (*N.elongata, N.parelongata*); tendency to resist Gram decolourisation; asporogenous; noncapsulated; nonmotile; some species fastidious; some species produce a yellow-green carotenoid pigment; oxidase positive, catalase produced (except *N.elongata*); most species reduce nitrite, some species oxidise carbohydrates; DNAse not produced; may be β-haemolytic; normal flora of mouth, nasopharynx, nose, external genitalia, anterior urethra, vagina (13%), eye, skin; causes pyogenic arthritis, bacteraemia and septicemia, human bite and clenched fist infections, meningitis, pyogenic osteomyelitis, otitis media (in infants), acute sinusitis; multiplies outside cells, but attachment to body surface necessary for invasion; growth stimulated by excess iron; infection increased by C5, C6, C7, C8 complement deficiency, sex hormones (menstrual cycle), absent serum bactericidal activity; primary immune defence prevention of attachment by coating microbial surface with specific antibody (mainly secretory IgA); neutralisation of microbial toxins also important; treatment: amoxycillin-clavulanate, cotrimoxazole, cefaclor; also susceptible to imipenem (100%), ciprofloxacin (MIC 0.07-0.015 mg/L), lomefloxacin (0.12 mg/L), enoxacin (0.12 mg/L), cefotaxime (0.12 mg/L), cefuroxime (1 mg/L), piperacillin (1 mg/L)

N.canis: cocci single and in pairs with adjacent sides flattened; CO_2 not required; no acid produced from carbohydrates; nitrate, but not nitrite, reduced; grows on nutrient agar at both 35°C and 25°C; no growth on Thayer-Martin medium; colonies smooth, butyrous and usually yellow pigmented; isolated from throats of cats and cat-bite wounds in humans

N.cinerea: cocci single and in pairs with adjacent sides flattened, CO_2 not required; acid from glucose, fructose and sucrose (may be negative in all), but not maltose or lactose; reduces nitrite (with gas), but not nitrate; grows on nutrient agar, trypticase soy agar, sheep blood agar and Muller-Hinton agar at both 35°C and 25°C and may grow on Thayer-Martin medium; isolated from throats of guinea pigs; causes bacteraemia and septicemia (uncommon in neutropenics and other immunodeficient), reported to cause proctitis in an 8 year old boy

N.elongata: short rods arranged as diplococci or in short chains; usually no acid produced from carbohydrates but some strains form weak acid in glucose; catalase usually negative; reduces both nitrate and nitrite (with gas); phenylalanine not deaminated; no growth on MacConkey agar; grows on nutrient agar at 35°C and 25°C; sparse growth on Thayer-Martin medium; weak yellow pigmented colonies occasionally show granular spreading zones; growth coherent, when collected lumpy and difficult to disperse; natural habitat nasopharynx of humans; isolated from bronchial aspirates, pus from perimandibular abscess and urine; considered a largely harmless parasite; cause of endocarditis and osteomyelitis

N.flavescens: cocci single but more often in pairs with adjacent sides flattened; CO_2 not required; no growth on Thayer-Martin medium or New York City medium, growth on brain heart infusion, usually slight growth at 22°C; usually grows on nutrient agar at both 35°C and 25°C; colonies smooth, opaque and usually yellow pigmented; no acid produced from carbohydrates; polysaccharides synthesised; reduces nitrite (with gas) but not nitrate; isolated from human trachea, lymph node and throat; a rare isolate; cause of meningitis, infective endocarditis (i.v. drug abusers with AIDS) and septicemia

N.gonorrhoeae: Gram negative, oval-shaped cocci single but more often in pairs with adjacent sides flattened and long axes parallel; oxidase and glucose positive; maltose, sucrose, fructose, mannitol, ONPG and γ-glutamyl aminopeptidase negative; nitrite, but not nitrate, occasionally reduced (no gas); growth on Thayer-Martin medium and New York City medium (most strains); no growth on brain heart infusion, trypticase soy agar or Mueller-Hinton agar; usually no growth on sheep blood agar; no growth at 22°C, no growth on nutrient agar at 35°C or 25°C; colonies opaque, grey-white, raised, granular, glistening and convex; gonococcal coagglutination and monoclonal antibody tests positive; obligate human parasite; isolated

from human cervix, vagina, blood, urethra, joint fluid, eye, urine, throat, CSF and rectum; causes gonorrhoea, anterior uveitis, septic arthritis (50% of total adult cases), bacteremia and septicemia, balanitis, 3% of carpal tunnel syndrome, mucopurlent cervicitis, purulent conjunctivitis, dermatitis, disseminated infection (dermatitis-polyarthritis syndrome with fever, sterile polyarthritis, tenosynovitis, pustular rash and bacteraemia; monoarticular syndrome with fever and suppurative monoarticular arthritis; intermediate forms), dysuria-frequency (urethral) syndrome, endocarditis, endometritis, acute epididymitis and epididymoorchitis, perinatal and prenatal generalised disease, neonatal and post-neonatal pyogenic meningitis, mycotic aneurism, oophoritis, parametritis, perihepatitis, peritonitis (primary), acute nonexudative pharyngitis and tonsillitis, proctitis, prostatitis and seminal vesiculitis, salpingitis, localised skin lesions, polymorphous rash, tenosynovitis, tubo-ovarian abscess, urethritis (acute and more severe in male), vaginitis, vulvovaginitis, infections in abnormal host, systemic infections in C5, 6, 7, 8 deficiency; sexually transmitted; defined peptide fragment on bacterial fimbriae (pili) attaches to carbohydrate polymer on urethral epithelium cell; infection generally confined to epithelial surface of urogenital tract; in disseminated gonorrhoea, ? ineffective antibody bound to microbe blocks action of 'good' antibody or immune cells; gonococcal bacteraemia usually caused by strains resistant to complement; inhibits phagocytic chemotaxis, attachment and ingestion, ingestion despite attachment, lysosome-phagosome fusion; IgA proteases interfere with IgA1; colony type 1 or 2, pili, lipopolysaccharide, capsule, IgA protease, AHU auxotype, ? LA factor associated with infection; colony types 3 and 4, no pili; persists in urogenital tract (infectious and shed to exterior), recovered or asymptomatic patient remaining infectious; 1000 genes; diagnosis: counterimmunoelectrophoresis (antigen and antibody), direct fluorescent antibody (skin lesion), culture on Transgrow, New York City medium (avoid cold, heat, lack of CO_2), coagglutination, PCR; susceptible to penicillin (in Australia, 6% resistance due to β-lactamase, 10% chromosomal resistance; significant geographic variation; total resistance up to 98% in Vietnam), ceftriaxone (resistance not yet reported), cefotaxime (MIC < 1 mg/L), erythromycin (1 mg/L), azithromycin, clarithromycin, roxithromycin, amoxycillin (β-lactamase negative), amoxycillin-clavulanate, tetracycline (5% high level resistance in Australia), cotrimoxazole, doxycycline, tetracycline, minocycline, chloramphenicol, spectinomycin (resistance not yet reported in Australia), ciprofloxacin (in Australia, 2% less susceptible, 2% resistant), gatifloxacin, moxifloxacin, norfloxacin (< 0.0125-0.12 mg/L), cefuroxime axetil, cefepime, cefpirome, ceftizoxime (< 1 mg/L), cefotetan, cefoxitin (≤ 0.125-1mg/L), ofloxacin (0.015-0.03 mg/L), rosoxacin (0.025 mg/L), enoxacin (≤ 0.06-0.12 mg/L), piperacillin (β-lactamase negative; 0.06mg/L), piperacillin-tazobactam, ticarcillin-clavulanate, mupirocin (0.06 mg/L), ampicillin (β-lactamase negative; 0.15 mg/L), apalcillin (β-lactamase negative; ≤ 0.5 mg/L), temocillin (β-lactamase negative; 0.5 mg/L), ticarcillin (β-lactamase negative; 0.5 mg/L), imipenem (100% susceptible at ≤ 1 mg/L), meropenem, cefoperazone (< 1 mg/L), moxalactam (< 1 mg/L), ceftazidime (< 1 mg/L), neomycin (1mg/L), cefixime

N.lactamica: cocci single, but more often in pairs with adjacent sides flattened; requires CO_2; growth on Thayer-Martin medium and New York City medium and on brain heart infusion, usually grows on nutrient agar at 35°C, few strains grow at 25°C, no growth at 22°C; colonies smooth, translucent, butyrous and usually yellow pigmented; glucose, maltose, lactose and ONPG positive; sucrose and fructose negative; reduces nitrite (with gas), but not nitrate; commonly found in nasopharynx of infants and children; isolated from human throat, nasopharynx, trachea, lung, sputum and vagina; rarely clinically significant; causes bacteraemia and septicemia (uncommon in neutropenics and other immunodeficient), postneonatal purulent meningitis following skull trauma; treatment: penicillin, cefotaxime, ceftriaxone

N.meningitidis: Gram negative, oval-shaped cocci single and in pairs with adjacent sides flattened and long axes parallel; requires CO_2; growth on New York City medium and on brain heart infusion, no growth at 22°C, no growth on nutrient agar at 25°C but a few strains grow at 35°C; colonies smooth, round and glistening; older cultures butyrous and rubbery; oxidase, glucose, maltose and γ-glutamyl aminopeptidase positive; lactose, sucrose, fructose, mannitol and ONPG negative; nitrite reduced by some strains (no gas), but not nitrate; obligate human parasite; increased respiratory carriage in epidemics; inapparent infections of pharynx or nasopharynx common; occasionally, mild inflammation causing pharyngitis and nasopharyngitis; isolated from human CSF, blood, petechiae, joints, throat, sputum, nasopharynx, eye and trachea; causes purulent conjunctivitis (rare), acute epididymitis and epididymoorchitis, gonorrhoea-like disease, post-neonatal meningitis (47% of meningococcal infections; ≈ 1000 cases/y in USA, 27% of bacterial meningitis cases, incidence 0.7/100 000 overall, 13/100 000 at age 3-8 mo; case-fatality rate 14%), meningococcemia (transient bacteraemia and chronic intermittent bacteraemia 43% of meningococcal infections, acute bacteremia and septicemia with or without meningitis, septicemic adrenal hemorrhage syndrome, hemorrhagic fever 5-20% of meningococcal infections; ≈ 300 cases/y in USA; incidence 0.2/100 000 overall, 5/100 000 at age 6-8 mo; case-fatality rate 25%), myocarditis and pericarditis, osteomyelitis and osteochondritis, peritonitis, septic arthritis (2% of meningococcal infections), polymorphous rash, localised skin lesions, spotted fever, pneumonia with exanthema (6% of meningococcal infections), otitis media (1% of meningococcal infections), supraglottitis (0.3% of meningococcal infections), infections in abnormal host (γ-globulin dysfunction, complement dysfunction, splenic dysfunction), systemic infections in agammaglobulinemia, complement deficiency, hyposplenism/splenectomy; total incidence in Australia ≈ 2/100 000 (15/100 000 in 0-4 y.o.); risk factors concomitant upper respiratory infection, crowding, climte, low economic status, bar patronage, college students living on campus, microbiologists working with the pathogen, travaellers to areas of high endemicity, military recruits, active and passive smoking, alcohol use, African American,

antibody deficiency syndromes, malignancies, chemotherapy, immunodeficiency, HIV infection, functional asplenia, congestive heart failure, diabetes mellitus, organ transplantion, male < 45 y, female > 45 y; in carrier state, attaches to respiratory epithelial cell by pili; inhibits phagocytic chemotaxis, attachment and ingestion; capsular polysaccharides virulence factor associated with invasiveness (Group A: N-acetyl-O-acetyl-mannosamine phosphate; Group B: N-acetyl-neuraminic acid; Group C: N-acetyl-O-acetyl-neuraminic acid); IgA proteases interfere with IgA1 (virulence factor); lipopolysaccharide (endotoxin) also associated with infection; primary bodily defence mechanism humoral immune responses (phagocytes +, alternative complement +, bactericidal activity +++, immune adherence (phagocytosis) +); recovery from primary infection due to antibody; diagnosis: counterimmunoelectrophoresis (antigen and antibody), direct fluorescent antibody (CSF), culture on Transgrow, Thayer-Martin medium, New York City medium (avoid cold, heat, lack of CO_2); susceptible to penicillin (in Australia, < 5% MIC > 1 mg/L), cefotaxime (≤ 0.06 mg/L), ceftriaxone (resistance not yet reported), cefepime, cefpirome, cefotetan, cefoxitin, amoxycillin (100% susceptible at 0.25 mg/L), doxycycline, tetracycline (0.5-1 mg/L), minocycline, ciprofloxacin (< 5% resistance in Australia), gatifloxacin, moxifloxacin, moxalactam (0.008-0.06 mg/L), cefperazone (0.008-0.12 mg/L), ofloxacin (0.15 mg/L), mupirocin (0.03 mg/L), pefloxacin (0.03 mg/L), cefixime (100% susceptible at ≤ 0.06 mg/L), cefuroxime (100% susceptible at ≤ 0.06 mg/L), ceftazidime (≤ 0.06 mg/L), ceftizoxime (0.06 mg/L), enoxacin (100% susceptible at < 0.12 mg/L), amoxycillin-clavulanate (100% susceptible at 0.12 mg/L), cefaclor (100% susceptible at 0.12 mg/L), rosoxacin (< 0.125 mg/L), ampicillin (0.2 mg/L), novobiocin (0.3 mg/L), hydroxynalidixic acid (0.5 mg/L), chloramphenicol (< 5% resistance in Australia), rifampicin (< 5% resistance in Australia), cephalothin (< 5% resistance in Australia), imipenem, meropenem

N.mucosa: cocci single and in pairs with adjacent sides flattened; CO_2 not required; colonies nonpigmented to yellowish, mucoid, adherent; glucose, maltose, sucrose and fructose positive; lactose negative; polysaccharides synthesised; reduces both nitrate and nitrite (with gas); usually grows on nutrient agar at both 35°C and 25°C; usually no growth on Thayer-Martin medium; natural habitat nasopharynx of humans; isolated from human blood, eye, CSF, wound, urine and sputum; occasionally pathogenic for humans; cause of pneumonia, ocular infection in a newborn, endocarditis (i.v. drug abuser), cellulitis, septic arthritis, abscess of Bartholin's gland, postneonatal purulent meningitis in female infants and children with predisposing conditions; treatment: penicillin, cefotaxime, ceftriaxone, amoxycillin, gentamicin, netilmicin

'N.parelongata': thin rods; variable growth on MacConkey; weak yellow pigmented colonies; carbohydrates not utilised; nitrite reduced (variable), but not nitrate; catalase produced; phenylalanine deaminated by most strains; associated with animal bite wounds of humans, pneumonia in an immunocompromised patient and osteomyelitis

N.polysaccharea: cocci arranged in pairs and tetrads with adjacent sides flattened; CO_2 not required; grows at 37°C but not 22°C; colonies yellow pigmented; acid produced from glucose and maltose, rarely from sucrose, but not from fructose or lactose; polysaccharides produced; ONPG not hydrolysed; nitrite, but not nitrate, reduced; nonhemolytic; isolated from pharynx of infants and children; clinical significance unknown

N.sicca: cocci single and in pairs with adjacent sides flattened; CO_2 not required; colonies nonpigmented (occasionally yellow pigmented), dry, wrinkled, adherent; growth at 22°C; usually grows on nutrient agar at both 35°C and 25°C; generally no growth on Thayer-Martin medium; glucose, maltose, sucrose and fructose positive; lactose, mannitol and ONPG negative; reduces nitrite (with gas), but not nitrate; natural habitat human nasopharynx, saliva and sputum; isolated from human throat, sputum, urine, blood and eye; rarely clinically significant; cause of pneumonia in immunodeficient patient, osteomyelitis following a back injury, endocarditis; treatment: penicillin

***Neisseria sp R-24680*:** coccoid to short rods; asporogenous; nonmotile; facultatively anaerobic; fastidious; variable growth on MacConkey; ferments glucose only (no gas); indophenol oxidase and catalase produced; reduces nitrate and nitrite, frequently with gas; most strains hydrolyse arginine and gelatine; phenylalanine usually deaminated; negative test reactions for urease and indole; cultures smell like popcorn; recovered from respiratory tract of animals; mostly associated with dog bites of humans

***Neisseria sp R-24681*:** coccoid to short rods; asporogenous; nonmotile; facultatively anaerobic; fastidious; variable growth on MacConkey; oxidises glucose only; indophenol oxidase and catalase produced; reduces nitrate and, sometimes, nitrite (no gas); phenylalanine usually deaminated; arginine and gelatine (usually) not hydrolysed; negative test reactions for urease and indole; cultures smell like popcorn; distinguished from *Neisseria sp R-24680* by oxidation of glucose and negative test reactions for arginine dihydrolase, gelatinase and gas from nitrate; natural habitat respiratory tract of dogs and cats; isolated from animal bite and scratch wounds of humans, endophthalmitis associated with cat scratch

N.subflava: cocci single and in pairs with adjacent sides flattened; CO_2 not required; colonies usually greenish yellow, smooth, transparent or opaque, often adherent; no growth on Thayer-Martin medium or New York City medium, growth on brain heart infusion; slight growth at 22°C, usually grows on nutrient agar at both 35°C and 25°C; glucose and maltose positive; lactose, mannitol and ONPG negative; sucrose and fructose variable; reduces nitrite (with gas), but not nitrate; agglutination in normal rabbit serum; natural habitat human nasopharynx; isolated from human throat, blood, CSF, sputum, nasopharynx, urogenital swab and eye; cause of bacteraemia and septicemia (neutropenics and other immunodeficient), endocarditis (i.v. drug abusers with AIDS) and postneonatal purulent meningitis; treatment: penicillin

Simonsiella: filamentous bacteria (6-8 μm long, 2-3 μm wide); consists of segmented groups of cells aligned face to face with their short axis coinciding with the long axis of the filament; asporogenous; obligately aerobic; grows on sheep blood agar and serum-enriched agar medium (BSTSY agar) at 37°C; no growth on MacConkey; narrow zone of haemolysis on blood agar; microcolonies detected after 6-10 h of incubation by scanning agar surface microscopically with a X10 objective lens and colonies subcultured at this time to prevent overgrowth by other flora; demonstrates gliding motility; catalase and indophenol oxidase produced; saprophyte in oral cavity of humans and a variety of warm-blooded vertebrates; causes erosive lesions of oral mucosa; susceptible to penicillin

Class Deltaproteobacteria

Order Desulfovibrionales

Family Desulfovibrionaceae

Bilophila wadsworthia: new genus and species

Desulfovibrio desulfuricans: motile, anaerobic, Gram negative bacillus, respiratory metabolism, sulphur compounds reduced to sulphur; normal flora of colon; causes sepsis, cholecystitis, intraabdominal abscess; susceptible to penicillin, clindamycin, chloramphenicol, tetracycline, erythromycin; resistant to vancomycin, colistin

D.piger: dissimilating sulphate-reducing bacteria

Class Epsilonproteobacteria

Order Campylobacterales

Family Campylobacteraceae

Arcobacter butzleri: causes diarrhoea, enterocolitis, bacteraemia and septicemia, appendicitis; treatment: ciprofloxacin

A.cryaerophilus: growth at 6°C and 25°C but not at 42°C; grows in 2% sodium chloride and 0.1% glycine, but not in 1% glycine; hippurate not hydrolysed; H_2S not detected in triple sugar iron agar; susceptible to nalidixic acid; cause of abortions in pigs, cattle, horses and sheep; found in the feces of a single patient with enteritis; occasionally isolated from human blood infections

Campylobacter: microaerophilic, vibrioid, slender, spirally coiled Gram negative rod; appears S-shaped and gull-winged when 2 cells form short chains; asporogenous; motile with a characteristic corkscrew-like motion by means of a single polar flagellum or a polar tuft of flagella at 1 or both ends; requires an oxygen concentration of 3-15% and a CO_2 concentration of 3-5%; serum or blood not required for growth; selective media required for isolation from mixed flora; optimum temperature usually 35°C; indophenol oxidase produced; carbohydrates neither fermented nor oxidised; nitrate reduced by most species; negative test reactions for urease (usually), gelatine and lipase; taxonomic problems exist at species level; normal flora of large intestine, reproductive organs and oral cavity of humans and animals; possibly the most prevalent bacterial pathogen; causes enteritis and enterocolitis (worldwide; often bloody diarrhoea and severe abdominal pain; 40% of faecal enteric pathogen isolates), 0.1% of bacteremia and septicemia, cholangitis and cholecystitis (rare), endocarditis, urinary tract infections including acute pyelonephritis, reactive arthritis (hips and lower back), Guillain-Barrè syndrome, stroke, subarachnoid hamorrhage, brain abscess, subdural empyema, nosocomial meningitis; zoonosis from poultry (gut organism in birds; sporadic disease) and milk (contamination by cow's faeces; outbreaks); also found in cats, dogs, goats, rabbits and a wide range of wild birds; attaches to intact epithelium; growth stimulated by excess iron; invasive infection plus enterotoxin; involves small intestine, colon and rectum; incubation period ? 3-5 d; treatment: erythromycin, cotrimoxazole, ciprofloxacin (MIC 0.03-0.5 mg/L); also susceptible to ofloxacin (1 mg/L), enoxacin (1 mg/L), imipenem (100%)

C.coli: characteristics as for *C.jejuni* but hippurate not hydrolysed; found in healthy pigs; causes diarrhoea, enterocolitis, abortion, fever, septic shock, stillbirth in humans

C.concisus: anaerobic, nonfermentative metabolism, succinic acid from fumarate; normal flora of oral cavity; associated with periodontal disease, single case of infected foot ulcer, uncommon cause of diarrhoea, enterocolitis; susceptible to imipenem (MIC $\leq$ 1 mg/L), ciprofloxacin ($\leq$ 1 mg/L), clindamycin, chloramphenicol, metronidazole, penicillin, tetracycline, erythromycin; resistant to vancomycin, bacitracin, rifampicin

C.faecalis: 2% NaCl and H_2S (TSI) positive, mean inhibitory zone size cephalothin > 40 mm, light growth in GasPak with catalyst at 37°C and 42°C; causes diarrhoea in cattle

C.fetus: causes abortion, abscesses, bacteraemia, intravascular infections, meningitis, prenatal generalised disease, stillbirth; inhibits phagocytic attachment and ingestion; transmission has been linked to tank water; treatment: gentamicin; also susceptible to pefloxacin (MIC 0.125-1 mg/L), amoxycillin-clavulanate (0.25-1 mg/L)

C.fetus subsp fetus: growth at 25°C, but usually not at 42°C; grows in 1% glycine, but not 3.5% NaCl; H_2S detected with lead acetate paper but not TSI agar; hippurate not hydrolysed; resistant to nalidixic acid; isolated from blood, CSF and pleural fluid of patients with various debilitating conditions; common cause of abortion in sheep and cattle, bacteraemia and septicemia, diarrhoea and enterocolitis in humans (usually compromised hosts); uncommon cause of septic abortion, septic arthritis, abscesses, endocarditis, neonatal and postneonatal purulent meningitis, mycotic aneurism, peritonitis, prenatal generalised disease, salpingitis and thrombophlebitis in humans; treatment: gentamicin, erythromycin, amoxycillin-clavulanate, piperacillin, cotrimoxazole, rifampicin, fluoroquinolone

C.fetus subsp venerealis: growth at 25°C, but not at 42°C; no growth in 1% glycine or in 3.5% NaCl; H_2S not detected with lead acetate paper or TSI agar; hippurate not hydrolysed; usually resistant to nalidixic acid; isolated from bovines; causes abortion and infertility in cattle; clinical significance in humans uncertain

C.gracilis: pitting colonies; vancomycin resistant, kanamycin susceptible, colistin susceptible, urease negative

C.hyointestinalis: growth at 42°C, variable growth at 25°C; grows in 1% glycine, but not in 3.5% NaCl; H_2S detected with both lead acetate paper and TSI agar; hippurate not hydrolysed; colonies yellow pigmented; resistant to nalidixic acid; causes proliferative ileitis in swine; occasionally found in faeces of patients with enteritis (watery diarrhoea) and enterocolitis; associated with proctitis

C.jejuni: grows only microaerophilically at 42°C, not at 25°C; mean inhibitory zone size nalidixic acid 32-36 mm, catalase and oxidase positive, H_2S detected with lead acetate paper but not TSI, darting/tumbling motility, growth in 1% glycine, no growth in 3.5% NaCl, hippurate hydrolysed; isolated from human stool and occasionally from blood and CSF; causes abortion in sheep, enteritis in cattle; common cause of colitis, diarrhoea, enteritis, enterocolitis, gastroenteritis in humans; uncommon cause of appendicitis, bacteraemia and septicemia (in conjunction with gastroenteritis in people at extremes of age or with cirrhosis, diabetes, renal failure, cancer, HIV; 8% of septicemia associated with female genital tract infection), female genital tract infection (3%), fever, Guillain-Barrè syndrome adult hepatitis, myocarditis, prenatal generalised disease, proctitis, reactive arthritis; rare cause of meningitis; found in 9% of adults and 19% of children with diarrhoea, 9% of asymptomatic children, absent in asymptomatic adults; attack rate (diarrhoea) 20-50% in day care centres; 6% of waterborne disease outbreaks (source human faeces; survival in water poor); 60% of cattle infected; transmitted in raw milk, chicken, salad vegetables, bottled water; replicates in intestinal epithelium, producing mucosal damage, inflammation and diarrhoea; toxin not demonstrated; susceptible to amoxycillin, ampicillin, azithromycin, clarithromycin, erythromycin (96% susceptible), roxithromycin, ciprofloxacin (MIC 0.25-1 mg/L), norfloxacin, nalidixic acid (100%), amikacin, gentamicin (100%), tobramycin, chloramphenicol (96%), imipenem, meropenem, pefloxacin (MIC 0.125-1 mg/L), fleroxacin (0.25-1 mg/L); variably susceptible to cefepime, ceftazidime; subsp *doylei* and *jejuni*

C.lari: growth at 42°C but not 25°C; grows in 1% glycine but not 3.5% NaCl; H_2S detected with lead acetate paper but not TSI agar; hippurate not hydrolysed; resistant to nalidixic acid; isolated from avian and mammalian species, most frequently from seagulls, occasionally from humans; causes diarrhoea and enteritis, bacteraemia and septicemia in humans; treatment: ciprofloxacin

C.sputorum: anaerobic, nonfermentative metabolism, succinic acid from fumarate; normal flora of nasopharynx, mouth, tooth surface, gingiva, saliva; associated with periodontal disease; causes abscesses; isolated from children with diarrhoea; susceptible to clindamycin, chloramphenicol, metronidazole, penicillin G, tetracycline, erythromycin; resistant to vancomycin, bacitracin, rifampicin

C.upsaliensis: growth at 42°C but not at 25°C; growth in 1% glycine; catalase reaction negative or weak; H_2S not detected with TSI agar; hippurate not hydrolysed; susceptible to cephalothin and nalidixic acid; isolated from dog, cat and human faeces; isolated from diarrhoeic and healthy hosts; clinical significance uncertain but considered an uncommon cause of diarrhoea, enterocolitis, bacteraemia and septicemia

Bacteroides ureolyticus: related to *Campylobacter*, pits surface of solid media; growth in broth containing 20% bile; vancomycin resistant, kanamycin susceptible, colistin susceptible; urease positive, esculin positive, indole negative, oxidase positive; normal flora of oropharynx, gastrointestinal tract, cervix, vagina, urethra; causes abdominal wound infection, severe erosive balanoposthtitis, empyema, infections of abdomen, blood, bone and soft tissue, head and neck, lungs and pleural space, intraabdominal abscess, lung abscess, non-specific urethritis, peritonitis, pneumonia, postoperative wound infection, submandibular abscess; 12% of anaerobes from perirectal abscess; susceptible to ciprofloxacin (MIC 0.06 mg/L), ofloxacin (0.12 mg/L), meropenem (0.13 mg/L), penicillin (0.25 mg/L), enoxacin (0.25 mg/L), norfloxacin (0.25 mg/L), difloxacin (0.5 mg/L), pefloxacin (0.5 mg/L), chloramphenicol, metronidazole

Family Helicobacteraceae

Helicobacter cinaedi: intermediate resistance to 30 μg cephalothin disc, nitrate positive, no odour, no growth at 25°C or 42°C, grows in 1% glycine but not in 3.5% NaCl, hippurate not hydrolysed, H_2S detected with lead acetate paper but not TSI agar, susceptible to nalidixic acid; isolated from human blood and rectal swabs; causes bacteremia and septicemia in AIDS, enteritis, enterocolitis, proctitis and proctocolitis in homosexual men

H.fennelliae: no growth at 25°C or 42°C; grows in 1% glycine but not in 3.5% NaCl; nitrate not reduced; hippurate not hydrolysed; H_2S detected with lead acetate paper but not TSI agar; distinctive hypochlorite odour; susceptible to nalidixic acid; sensitive to 30 μg cephalothin disc; nitrate negative; isolated from human blood and rectal swabs; associated with bacteremia and septicemia, diarrhoea, enteritis, enterocolitis, proctitis and proctocolitis in homosexual men

H.pylori: curved Gram negative bacillus, rods sometimes 'oxbow' shaped, cells large compared with *Campylobacter*, polar flagella; requires CO_2, blood or serum and adequate surface moisture for growth; enriched medium, chocolate agar or selective enriched medium used for isolation from biopsy tissue; does not grow anaerobically; some strains grow poorly at 30°C and 40°C; 3.5% NaCl, glucose, indole and nitrate negative; 1% glycine, oxidase and catalase positive; produces urease, H_2S detected with lead acetate paper, hippurate not hydrolysed, resistant to nalidixic acid; causes antral gastritis, duodenal and

peptic ulcers, mucosa-associated lymphoid tissue lymphoma, ? syndrome X (microvascular angina), primary migraine, primary Raynaud's phenomenon, ischaemic heart disease; reservoir in dental plaque; transmission person-to-person (oral-oral, fecal-oral), possibly water-borne in some locations; seroprevalence in Australia 30.6%, ≈ 50% in USA, ≈ 90% in developing countries; treatment: combinations of proton pump inhibitors + bismuth salt + metronidazole or tinidazole or amoxycillin + clarithromycin or tetracycline; also susceptible to penicillin G, erythromycin, gentamicin, cephalothin

Wolinella succinogenes: anaerobic, polar flagella, nonfermentative, produces succinic acid from fumarate

Class Gammaproteobacteria

Order Aeromonadales

Family Aeromonadaceae

Aeromonas: straight rods; asporogenous; motile by a single polar flagellum; facultatively anaerobic (metabolism of glucose both respiratory and fermentative); grows at 35°C; most routine laboratory media, including MaConkey and SS agar, support growth; colonies round, raised, with an entire edge, smooth surface, white to buff; oxidase positive; catalase produced; resistant to vibriostatic agent 2,4-diamino-6,7-diisopropylpteridine (O/129); acid or acid and gas produced from glucose, maltose, mannitol and other carbohydrates, but not xylose; positive test reactions for indole, nitrate (no gas), lecithinase, amylase, gelatinase, deoxyribonuclease, arginine dihydrolase, O-nitrophenyl-β-D-galactopyranoside hydrolysis and growth in broth without NaCl; negative test results for H_2S, urease, phenylalanine deaminase and growth in broth with 6.5% NaCl; variable test reactions for lysine decarboxylase and ornithine decarboxylase; psychrotrophic, nonmotile aeromonads not recovered from humans differ from mesomorphic, motile aeromonads in a number of additional phenotypic properties; routine identification of mesophilic, motile aeromonads to species level is not recommended; mesophilic, motile aeromonads occur widely in water, sludge and sewage; causal agent of 'red-leg' disease in amphibians, diseases in reptiles, fish, snails, cows and humans; opportunistic for immunologically compromised patients suffering from chronic disease; occasionally primary agents of disease; normal flora of large intestine, lower ileum; causes diarrhoea (enterotoxigenic strains (predominantly *A.hydrophila* and *A.veronii* biotype sobria) watery to cholera-like diarrhoea by possession of adhesins and action of cytotoxic and/or cytotonic enterotoxins on small intestine; enteroadherent strains (*A.caviae)* watery diarrhoea especially in infants < 1 mo by possession of adhesins and ? action of enterotoxins on small and large intestine; enteroinvasive strains (*A.veronii* biotype sobria > *A.hydrophila*) severe diarrhoea and dysentery to colitis, fever, faecal leucocytes by possession of adhesins and invasins and action of cytotoxic enterotoxins on large intestine), abortional infection, bacteraemia and septicemia (uncommon in neutropenics), endocarditis, localised skin lesions in septicemia and endocarditis (often fatal), endophthalmitis (foreign body trauma), infection of skin, soft tissue, muscle and bone associated with traumatic exposure to water, local and generalised sepsis (cellulitis, myonecrosis with or without gas gangrene, ecthyma gangrenosum), neonatal meningitis, 0.1% of nosocomial infections (0.3% of Gram negative bacilli), osteomyelitis and osteochondritis, otitis, peritonitis (nosocomial), postoperative complications, thrombophlebitis, urinary tract infection (occasional); 48% of clinical isolates from gastrointestinal tract, 19% from wounds, 13% from blood; growth stimulated by excess iron; susceptible to amikacin, gentamicin, tobramycin, ciprofloxacin (< 5% resistance in Australia), fleroxacin (MIC ≤ 0.06-0.12 mg/L), gatifloxacin, moxifloxacin, ofloxacin (0.1 mg/L), norfloxacin (0.1- 0.5 mg/L), enoxacin (0.13-0.5 mg/L), usually susceptible to chloramphenicol, cotrimoxazole, trimethoprim, doxycycline, tetracycline, minocycline, aztreonam, trimethoprim; all isolates produce an inducible penicillinase and mutate at a relatively high frequency to produce this enzyme constitutively, resulting in high level resistance to all penicillins, and should be regarded as resistant to all penicillins; 95% of strains mutate at a high rate to resistance to imipenem; many strains also produce an inducible cephalosporinase and can mutate to produce this enzyme constitutively, resulting in high level resistance to all β-lactams except imipenem

A.eucrenophila: new species

A.hydrophila: faculatively anaerobic motile Gram negative bacillus; β-haemolytic; non-lactose fermenting on MacConkey with cloudy pink halo; growth on SS; oxidase, catalase, H_2S, esculin, glucose (no gas), mannitol, maltose, sucrose, salicin, arabinose, VP, gluconate, arginine dihydrolase, indole, nitrate, lecithinase and elastase positive; inositol, sorbitol, rhamnose, melibiose, ornithine decarboxylase and urease negative; KCN, lactose and lysine decarboxylase variable; 'indigenous' to freshwater; occasionally pathogenic for frogs, fish and mammals, including humans; isolated from human stool, blood, wound and respiratory tract; causes bacteraemia and septicemia (≈ 50% case-fatality rate in immunocompromised), traumatic and aquatic wound infections, skin and soft tissue infections (water-related), cellulitis (± bullae, abscesses and crepitant, necrotising myonecrosis), multiple abscesses in immunodeficient persons, traveller's diarrhoea, enteritis, gastroenteritis, pneumonia, infections in abnormal host; treatment: gentamicin (100% susceptible), ciprofloxacin (100% susceptible at 0.015 mg/L); also susceptible to ofloxacin (100% at 0.015 mg/L), enoxacin (0.015-0.12 mg/L), pefloxacin (0.06 mg/L), norfloxacin (100%), cotrimoxazole (90%), tobramycin, amikacin, chloramphenicol, tetracycline; should be regarded as resistant to all β-lactams and imipenem

A.jandaei: causes gastroenteritis, septicemia, wound infections

A.media: psychrotrophic; nonmotile; esculin, KCN, salicin, arabinose and arginine dihydrolase positive; no gas from glucose; VP, gluconate, lysine decarboxylase, lecithinase and elastase negative; not recovered from humans

A.punctata: not β-hemolytic; oxidase, esculin, KCN, salicin, arabinose and arginine dihydrolase positive; ferments glucose (no gas) and mannitol; gluconate, ornithine decarboxylase, urease, lecithinase and elastase negative; found in fresh water and sewage and on fish; isolated from human stool, blood, wound and respiratory tract; causes gastroenteritis (particularly pediatric); susceptible to meropenem (MIC $\leq$ 0.06 mg/L), cotrimoxazole, tetracycline, gentamicin; resistant to ampicillin, cephalothin

A.salmonicida: psychrotrophic; nonmotile; no growth at 37°C; brown pigment; methyl red and gelatine positive; VP, Simmon's citrate, inositol and urease negative; causes fish furunculosis, ulcer disease; not recovered from humans

A.schubertii: causes traumatic aquatic wound infections

A.veronii biovar sobria: β-hemolytic; H_2S, gas from glucose, gluconate, arginine dihydrolase, lysine decarboxylase, lecithinase and elastase positive; esculin, KCN, salicin, arabinose, urease and ornithine decarboxylase negative; VP reaction strain variable; found in fresh water and sewage and on fish; isolated from human stool, blood, wound and respiratory tract; causes gastroenteritis (? invasive), postneonatal pyogenic meningitis in chronic alcoholic liver disease (rare), septicemia, wound infections; 30% of clinical isolates; susceptible to meropenem (MIC 1 mg/L), cotrimoxazole, gentamicin; resistant to ampicillin

A.veronii biovar veronii: gas from glucose, salicin fermented, VP reaction positive, growth in KCN broth strain variable, esculin hydrolysed, ornithine decarboxylated; isolated from human stool, sputum, wound, maxillary sinus, endotrachea and leg; causes gastroenteritis and septicemia

Family Succinivibrionaceae

Anaerobiospirillum succiniciproducens: bipolar tufts of flagella; causes septicemia, diarrhoea; treatment: cephamandole; also susceptible to cephalothin, chloramphenicol, tetracycline, rifampicin; resistant to vancomycin, trimethoprim, penicillin

Ruminobacter amylophilus: normal flora of gastrointestinal tract

Succinimonas amylolytica: motile by polar flagella, anaerobic, Gram negative bacillus, ovoid cells, succinic acid produced, fermentative; single case of groin cellulitis and abscess; susceptible to bacitracin, oxytetracycline, penicillin; resistant to kanamycin, streptomycin, erythromycin

Succinivibrio: obligately anaerobic Gram negative rods, spiral-shaped cells, nonsporeforming, motile by polar flagella, fermentative, produces succinic acid

S.dextrinosolvens: motile, anaerobic, Gram negative bacillus, spiral cells, succinic acid produced; normal flora of oral cavity, colon; rare cases of septicemia (associated with gastrointestinal or oesophageal sepsis); susceptible to penicillin, tetracycline, erythromycin, chloramphenicol

Order Alteromonadales

Family Alteromonadaceae

Alteromonas putrefaciens: straight or curved rods, asporogenous; motile by a single polar flagellum; obligately aerobic; indophenol oxidase and catalase produced; indole not formed; oxidative in carbohydrates; colonies slightly viscous or mucoid and usually red-brown or pink in colour; produces abundant H_2S in Kligler iron agar; highly proteolytic; ornithine decarboxylase and DNAse tests positive; nitrate reduced (no gas); no PHB; distinguished from phenotypically similar strains of *Shewanella putrefaciens* on basis of oxidation of sucrose and maltose and failure to grow in high salt concentration (6.5%); however, sodium ion required for growth (no growth in 0% NaCl medium); found primarily in dairy, fishery and other environmental sources; isolated from eggs, butter, cuttlefish, haddock, cod, cutting oil, frog liver, ground beef, poultry, ditch water, tap water, sea water and sewage; causes spoilage of protein foods stored at refrigerator temperature, including butter, fish, meat and poultry; isolated from human pleural fluid, CSF, nose, throat, sputum, urine and blood; rarely clinically significant; associated with an intraabdominal abscess in a patient with colonic carcinoma; isolated from bile of a patient with biliary tract disease

Family Shewanellaceae

Shewanella putrefaciens: colonies slightly viscous or mucoid and usually red-brown or pink in colour; motile with a single polar flagellum; produces abundant H_2S in Kligler iron agar; indophenol oxidase produced; reduces nitrate (no gas); highly proteolytic; ornithine decarboxylase and DNAse tests positive; distinguished from phenotypically similar strains of *Alteromonas putrefaciens* by failure to produce oxidative acidity from sucrose and maltose and ability to grow in high salt concentration (6.5%); few environmental isolates; primarily isolated from human blood, ear, urine, feces, sputum, pus, wound exudate and throat; causes fish spine injury infection, cellulitis; an occasional opportunist associated with otitis media, meningitis following head injury, lower limb cellulitis, bacteremia and septicemia in patients with chronic infection of lower extremity and in association with severe underlying debility, liver disease, malignancy; usually susceptible to gentamicin, neomycin, nitrofurantoin, kanamycin, nalidixic acid, erythromycin, polymyxin B, tetracycline, chloramphenicol, cotrimoxazole

Order Cardiobacteriales

Family Cardiobacteriaceae

Cardiobacterium hominis: pleomorphic rods; variable rosette clusters; tendency to retain crystal violet stain; asporogenous; nonmotile; facultatively anaerobic; fastidious; no growth on MacConkey; growth enhanced by increased

moisture and CO_2; colonies intertwining network of bacilli comprising colony core with peripheral streaming of filamentous bacilli, frequently pit agar surface; ferments glucose (no gas), mannitol, sucrose and maltose, but not xylose or lactose; indophenol oxidase, but not catalase, produced; indole (weak) formed; negative test reactions for urease and nitrate; rare mannitol negative strains distinguished from phenotypically similar *Kingella indologenes* strains by positive tests for caseinase, phosphatase and Tween 40 hydrolysis by the latter; found in nasopharynx and sputum of apparently healthy persons; also occurs in faeces; causes bacteraemia, endocarditis, meningitis; treatment: penicillin, cephalosporins, tetracycline

Dichelobacter nodosus: large pleomorphic cells; Gram negative; obligate anaerobe; causes footrot in sheep

Suttonella indologenes: rods more regular, longer in shape and evenly stained compared with *Kingella* species; ferments glucose, maltose and sucrose; indole produced; negative test reactions for growth on MacConkey, nitrate and nitrite reduction; may pit agar surface; rare mannitol negative strains of *Cardiobacterium hominis* distinguished from strains of *S.indologenes* on basis of casein hydrolysis, phosphatase production and Tween 40 hydrolysis by the latter; natural habitat mucous membranes of respiratory tract of humans; causes endocarditis (rare), conjunctivitis, corneal abscess

Order Enterobacteriales

Enterobacteriaceae: facultatively anaerobic Gram negative bacteria; motile and nonmotile; nonsporeforming; indophenol oxidase negative; reduce nitrates to nitrites; ferment glucose, forming acid alone or acid and gas; growth on MacConkey, growth on SS; lysine decarboxylase, arginine dihydrolase and ornithine decarboxylase usually negative; normal flora of mouth, throat, large intestine, lower ileum, external genitalia, anterior urethra, vagina; cause abscesses, bacteremia, bacteriuria, cystitis, diarrhoea, endocarditis, enteric fevers, intoxication, lung abscesses, meningitis, 15% of necrotising fascitis, peritonitis, pneumonia, postoperative and posttraumatic complications, pyelonephritis, prostatitis and seminal vesiculitis, septicaemic adrenal syndrome, thyroiditis, infections in patients with interrupted integument, surgical procedure, neutrophil dysfunction; immunity due to phagocytes (+++), complement (+), antibody (+); synthesise lipopolysaccharides, not teichoic acid; form rough colonies on loss of O antigens; susceptible to carumonam (MIC $\leq$ 0.125 mg/L), aztreonam ($\leq$ 0.125 mg/L), enoxacin ($\leq$ 0.125-1 mg/L), norfloxacin (0.25-1 mg/L), imipenem (< 5% resistance in Australia), amikacin (< 5% resistance in Australia); 100% intrinsic resistance to penicillin, flucloxacillin, clindamycin, erythromycin

Citrobacter: glucose (with gas), H_2S, rhamnose, arabinose, sorbitol and citrate positive; indole, lysine decarboxylase and urea negative; lactose, malonate and dulcitol variable; causes bacteraemia, asymptomatic bacteriuria (frequently extraneous), urinary tract infection, perinatal generalised infection, wound infection, suppurative lesions; some strains appear to cause occasional outbreaks of enteritis; some strains Vi antigen positive; treatment: gentamicin, chloramphenicol; also susceptible to ciprofloxacin (MIC 0.015-0.25 mg/L), enoxacin (0.125-0.5 mg/L), amifloxacin (0.125-0.5 mg/L), ofloxacin (0.25 mg/L), pefloxacin (0.25 mg/L), lomefloxacin (0.5 mg/L), norfloxacin (1 mg/L); 98% intrinsic resistance (due to inducible Class I chromosomal β-lactamase) to amoxycillin, ampicillin, amoxycillin-clavulanate, cephalothin, cephazolin, cephalexin (possibly all resistant in clinical practice; should be considered resistant to all cephalosporins, penicillins, cephamycins and aztreonam, but may be susceptible to imipenem)

C.amalonaticus: susceptible to ciprofloxacin (100%), norfloxacin (100%), enoxacin (100%), meropenem (MIC $\leq$ 0.06 mg/L)

C.diversus: adonitol, malonate, indole, arginine dihydrolase (may be delayed), ornithine decarboxylase, mannitol and salicin (may be delayed) positive; KCN, H_2S and lysine decarboxylase negative; urease variable; causes infections in abnormal host, neonatal nosocomial meningitis (brain abscess common); treatment: cefotaxime, ceftriaxone, chloramphenicol; also susceptible to ofloxacin (MIC $\leq$ 0.03-0.5 mg/L), pefloxacin (0.03-0.5 mg/L), meropenem ($\leq$ 0.06 mg/L), ciprofloxacin (100% susceptible at 0.06 mg/L), enoxacin (0.25 mg/L), norfloxacin (0.25 mg/L), gentamicin (0.5 mg/L), usually susceptible to cotrimoxazole, trimethoprim, amikacin, tetracycline

C.freundii: KCN and mannitol positive; lysine decarboxylase negative; urease, ornithine decarboxylase, lactose, salicin and raffinose variable; isolated from water; species most commonly found in patients; causes infections in abnormal host, perianal and perirectal abscess and cellulitis in patients with malignant disease, peritonitis; susceptible to piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, cefuroxime, cefepime, cefpirome, ceftazidime, meropenem (0.13 mg/L), ciprofloxacin (100% at 0.25 mg/L), gatifloxacin, moxifloxacin, norfloxacin (99%), enoxacin (98% at 0.25 mg/L), ofloxacin (0.25 mg/L), difloxacin (0.5 mg/L), imipenem (100%), aztreonam, cotrimoxazole, trimethoprim, amikacin, gentamicin, tobramycin; 96% intrinsic resistance to amoxycillin and ampicillin, 92% to amoxycillin-clavulanate, 97% to cephalothin, cephazolin and cephalexin (possibly all resistant in clinical practice)

Edwardsiella tarda: lysine decarboxylase, ornithine decarboxylase, glucose (with gas), H_2S and indole positive; Simmon's citrate, KCN, lactose, urease, sucrose, mannitol, dulcitol, salicin, adonitol, inositol, sorbitol, raffinose and rhamnose negative; arabinose variable; isolated from water and human wounds; causes bacteremia and septicemia, cellulitis associated with trauma to mucosal surfaces, infection in abnormal host, intestinal and extraintestinal infections similar to those caused by *Salmonella,* wound infections and necrosis (60% after exposure to marine environment), felon, tubo-ovarian abscess, Bartholin abscess, perirectal abscess, cholecystitis; risk factors include exposure to aquatic environments or exotic animals, preexisting liver disease, iron overload, raw fish ingestion; > 90% of phenotypes show invasion of HeLa and Hep-2 cells and complement-mediated resistance and produce β-hemolysis and chondroitinase, 50% have non-fimbrial adhesins, 10% produce enterotoxin and some produce dermatonecrotic toxin; treatment: ciprofloxacin

Genus Chronobacter

Enterobacter sakazakii: isolated from water and human wounds; rare invasive infections with high death rate in neonates; DNAse positive at 25°C at 24-48 h; susceptible to ciprofloxacin (MIC ≤ 0.06 mg/L), meropenem (0.13 mg/L), enoxacin (0.25 mg/L), norfloxacin (0.25 mg/L)

Enterobacter: arabinose, mannitol, rhamnose and citrate positive; malonate variable; causes 1-3% of bacteremia and septicemia, cholangitis and cholecystitis, emphysematous gastritis, human bite and clenched fist infections, endophthalmitis, mycotic aneurism, 4% of nosocomial infections, osteomyelitis and osteochondritis, pneumonia (mainly nosocomial), acute empyema, local and generalised sepsis, thrombophlebitis, urinary tract infections (acute cystitis); extracellular; growth stimulated by excess iron; K antigens, O antigens and endotoxin virulence factors; major host defence mechanisms phagocytes (+), alternative complement (+), bactericidal activity (+), immune adherence (phagocytosis) (+++); susceptible to ciprofloxacin (2% resistance in Australia), gatifloxacin, moxifloxacin, enoxacin (0.125-0.5 mg/L), amifloxacin (0.25 mg/L), norfloxacin (0.8% resistance in hospitals and 3% in private laboratories), ofloxacin (92% sensitive at 0.5 mg/L), lomefloxacin (0.5 mg/L), imipenem (2% resistance in hospitals, none so far in private laboratories), meropenem, pefloxacin (1 mg/L), mezlocillin, tobramycin, chloramphenicol, cotrimoxazole (5% resistance in hospitals and 7% in private laboratories), trimethoprim (8% resistance in hospitals and 12% in private laboratories), gentamicin (3% resistance in hospitals and 1% in private laboratories), amikacin, ticarcillin, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, cefepime, cefpirome, azlocillin; 96% intrinsic resistance (due to β-lactamase) to amoxycillin and ampicillin, 92% to amoxycillin-clavulanate, 97% to cephalothin, cephazolin, and cephalexin (possibly all resistant in clinical practice); in Australia, 25% resistance to cefotaxime, ceftriaxone and ceftazidime in hospitals and 10% in private laboratories

E.aerogenes: VP, ornithine decarboxylase, sucrose, salicin, inositol, sorbitol, raffinose, lysine decarboxylase, mucate, glucose (with gas) and lactose positive; methyl red, urease, indole and H_2S negative; gelatine variable; motile; common in human intestinal tract; causes infections in abnormal host; on occasion, may be opportunistic pathogen and cause suppurative lesions at almost any site; primary bodily defence mechanism leucocyte bactericidal function; susceptible to carumonam (0.12-0.5 mg/L), meropenem (0.13 mg/L), oxolinic acid (≤ 0.25 mg/L), pefloxacin (0.25 mg/L), difloxacin (0.5 mg/L), ciprofloxacin (98% of hospital isolates), norfloxacin (100%), ofloxacin (100%), imipenem (96% of hospital isolates), enoxacin (94%), gentamicin (98% of hospital isolates), tobramycin (100%), amikacin, cotrimoxazole (98% of hospital isolates)

E.cancerogenus: isolated from water and human wounds; causes typhlitis

E.cloacae: VP, arginine dihydrolase, ornithine decarboxylase, mucate, glucose (with gas), lactose (may be delayed), sucrose, sorbitol, raffinose and salicin (may be delayed) positive; methyl red, indole and H_2S negative; gelatine, dulcitol and inositol variable; motile; isolated from water and human wounds; causes bursitis, infusion infections, perianal and perirectal abscess and cellulitis in patients with malignant disease, perinatal generalised disease, peritonitis; on occasion, may be opportunistic pathogen and cause suppurative lesions at almost any site; treatment: gentamicin (14% resistance in Australia), chloramphenicol; also susceptible to ciprofloxacin (5 % resistance in Australia, 11% in USA), imipenem (2% resistance in Australia), ofloxacin (100% at 0.25 mg/L), meropenem (0.25 mg/L), rosoxacin (0.8 mg/L), norfloxacin (1% resistance in Australia, 14% in USA), enoxacin (98%), tobramycin (95% of hospital isolates), cotrimoxazole (12% resistance in Australia, 17% in USA), trimethoprim (23% resistance in Australia); possesses an inducible Class I chromosomal β-lactamase and should be considered resistant to all cephalosporins, penicillins, cephamycins and aztreonam but may be susceptible to imipenem

Erwinia: causes rare opportunistic infections in abnormal host (including bacteremia and septicemia in neutropenics), nosocomial infections

Escherichia: Gram negative rods; usually motile; indole, lactose and lysine decarboxylase positive; citrate negative; gas from glucose; normal flora of vagina (4%); growth stimulated by excess iron; susceptible to ciprofloxacin (MIC 0.015-0.5 mg/L)

E.coli: Gram negative, motile bacilli; indole, glucose, lactose, mannitol, arabinose and β-glucuronidase on 4-nitrophenyl-β-D-glucopyranosiduronic acid positive; acid and gas, but not hydrogen sulphide, produced on triple sugar iron agar slant; Simmon's citrate and potassium cyanide negative; ornithine decarboxylase, lysine decarboxylase, arginine dihydrolase, dulcitol, salicin, sorbitol, raffinose and rhamnose variable; normal flora of colon in man and animals, cervix (20%); many antigenic types; causes 12-29% of bacteraemia and septicemia, asymptomatic bacteriuria, acute bronchitis in newborn, bursitis, cholecystitis and cholangitis, purulent conjunctivitis, acute cystitis (72% of all cases), infantile and traveller's diarrhoea, acute empyema, endocarditis, endometritis, endophthalmitis (bloodborne), endotoxic reactions associated with reuse of cardiac catheters, acute epididymitis and epididymoorchitis, chronic eye infections, emphysematous gastritis, gastroenteritis, haemorrhagic colitis, haemolytic uraemic syndrome, adult hepatitis, human bite and clenched fist infections, intraabdominal abscess, mastitis and breast abscess, meningitis in neonates and adult immunocompromised, neonatal necrotising enterocolitis, nosocomial infections (13% of total, 34% of urinary tract infections, 17% of septicemia, 23% of Gram negative bacilli), osteomyelitis and osteochondritis, 2% of otitis externa, parametritis, pelvic abscess, pelvic inflammatory disease, perianal and perirectal abscess and cellulitis in patients with malignant disease, perinatal generalised disease, peritonitis (primary, secondary, spontaneous, peritoneal dialysis), primary and secondary pneumonia, prostatitis and seminal vesiculitis (older patients), acute pyelonephritis, rhabdomyolysis, salpingitis, septic arthritis, acute sinusitis, localised skin lesions in septicemia

and endocarditis, local and generalised sepsis, 15% of surgical wound infections, symbiotic gangrene, nasal septic abscess, splenic abscess, 8% of thrombophlebitis, tubo-ovarian abscess, typhlitis, endogenous and nosocomial urinary tract infections, 16% of vascular graft infections, infections in abnormal host, systemic infections in granulocytopenia; attaches to intestinal epithelium (requires specific bacterial surface components on fimbriae (piglet: pilus K88 antigen; calves: K89 antigen; humans: ? K antigen), attaching to D-mannose receptor; infantile gastroenteritis strains (enteropathogenic *Escherichia coli* (632 M cases with 389 000 deaths (90% in children < 5 y) globally annually) express intimin protein that binds to host epithelium and stimulates an immunopathologic response favouring colonisation, cause diarrhoea by an unknown mechanism and show localised adherence to tissue culture cells by a plasmid-borne adhesin; traveller's diarrhoea strains (enterotoxigenic *Escherichia coli*; plasmid-borne tox gene; 744-1000 M episodes resulting in 4-6 M deaths in Africa, Latin America and Asia excluding China annually) attach to small intestine by colonisation factor antigen—sialic acid-specific lectin binding to tissue 2-8,N-acetyl-neuraminic acid, rarely penetrate, and cause diarrhoea by forming either heat-stable or heat-labile enterotoxin or both, which induce fluid loss from epithelial cells (disease-producing dose 10^6-10^9; food and water (source human faeces; survival 5h - 2 d) transmission; produce profuse watery diarrhoea, no blood in stool; in less developed countries and in travellers); coliform enteritis or dysentery (abdominal cramps, tenesmus, usually blood in stool) and piglet diarrhoea strains (enteroinvasive *Escherichia coli*) show ability to invade epithelial cell lines or conjunctiva of animals (plasmid-borne via genes), initially localise in small bowel, later attach to and penetrate epithelium of large intestine, multiplying intraepithelially and inducing mucosal inflammation, ulceration of mucosa and diarrhoea; calf enteritis strains attach to and penetrate epithelium of small intestine and invade subepithelial tissues; enterohaemorrhagic strains produce a toxin closely related to that produced by *Shigella dysenteriae* serotype 1 (verocytotoxin or Shiga-like toxin), encoded by a bacteriophage and causing haemorrhagic colitis, occasionally complicated by haemolytic uraemic syndrome; enteroaggregative strains cause nonspecific diarrhoea, traveller's diarrhoea and persistent diarrhoea, and show an aggregative pattern of adherence to cell cultures by a plasmid-borne adhesin), urinary tract epithelium (pili adhere to D-mannose receptor); multiplies outside cells but attachment to body surface necessary for invasion; selective adherence to small bowel, pharynx, buccal mucosa, urogenital tissue (low adherence to labium majus); inhibits phagocytic chemotaxis, attachment and ingestion, oxidative attack; capsular acid K antigens, cell wall O antigens and pilus protein K antigens associated with invasiveness; M antigens also present; K1 antigens, O antigens, pilus protein, endotoxin and haemolysin virulence factors; K1 antigen similar to group B *Neisseria meningitidis* antigen and similarly associated with meningitis; serogroups O26:NM, O55:NNM, O55:H6, O55:H7, O86:NM, O86:H2, O86:H34, O111:NM, O111:H2, O111:H12, O111:H21, O114:NM, O114:H2, O119:H6, O125ac:H21, O126:H27, O127:NM, O127:H6, O127:H9, O127:H21, O128ab:H2, O142:H6, O158:H23 enteropathogenic; serogroups O6:H16, O8:NM, O8:H9, O11:H27, O15:H11, O20:NM, O25:NM, O25:H42, O27:H7, O27:H20, O63:H12, O78:H11, O78:H12, O85:H7, O114:H21, O115:H21, O115:H40, O126:H9, O128ac:H7, O128ac:H12, O128ac:H21, O148:H28, O149:H4, O159:H4, O159:H20, O166:H27, O167:H5 enterotoxigenic; serogroups O28ac:NM, O29:NM, O112ac:NM, O115ac:NM, O124:NM, O124:H7, O124:H30, O135:NM, O135:NM, O143:NM, O144:NM, O144:H25, O152:NM, O165:NM, O167:NM enteroinvasive; serogroups O26:H11, O157:H7 enterohaemorrhagic; serogroups ONT:H33, O3:H2 enteroaggregative; primary immune defence immune adherence (phagocytosis) (+++), phagocytes (+), alternative complement (+), prevention of attachment by coating microbial surface with specific antibody (mainly secretory IgA) (+), bactericidal activity (+), neutralisation of microbial toxins also important; 4288 genes; mean doubling time 20 minutes in vitro; detection of toxin: ELISA; susceptible to ticarcillin-clavulanate, gentamicin (in Australia, 0.9% resistance), chloramphenicol, cephalexin, cefaclor, cefuroxime, cefotaxime and ceftriaxone (0.1% resistance), cefepime, cefpirome (MIC 0.03-0.6 mg/L), cefotetan, cefoxitin, rosoxacin (0.05 mg/L), meropenem (≤ 0.06 mg/L), ofloxacin (96% susceptible at 0.06 mg/L), cefmenoxime (0.06-0.12 mg/L), aztreonam (1% resistance in hospitals), carumonam (0.06-0.12 mg/L), foramidocillin (0.12-0.5 mg/L), amifloxacin (0.125 mg/L), pefloxacin (0.125-0.25 mg/L), amdinocillin (0.13 mg/L), ciprofloxacin (0.3% resistance in Australia, 4% in USA), gatifloxacin, moxifloxacin, cefixime (≤ 0.25 mg/L), lomefloxacin (0.25 mg/L), ceftizoxime (100% susceptible at 1 mg/L), imipenem (0.1% resistance in Australia), enoxacin (99% susceptible at 1 mg/L), norfloxacin (0.3% resistance in Australia, 4% in USA), ceftazidime (1% resistance in hospitals), moxalactam (< 1 mg/L), neomycin, soframycin, amikacin, tobramycin (1% resistance in hospitals), piperacillin-tazobactam (3% resistance in hospitals), levofloxacin (4% resistance in USA), nitrofurantoin (2% resistance in USA); 48% resistance (due to β-lactamase) to amoxycillin, ampicillin (39% in USA), ticarcillin, piperacillin, azlocillin, 19% resistance to cotrimoxazole, 19% resistance to trimethoprim, 32% resistance (due to β-lactamase) to cephalothin (30% in USA), 13% to cephazolin and 7% to cephalexin, 27% resistance (due to β-lactamase) to amoxycillin-clavulanate (17% in USA)

Hafnia alvei: lysine decarboxylase, ornithine decarboxylase and gas from glucose positive; gelatine and mucate negative; methyl red, VP, Simmon's citrate, arginine dihydrolase, lactose and sucrose variable; found in human intestinal tract but is not enteropathogenic; on very rare occasions, causes infections in abnormal host (including bacteremia and septicemia in neutropenics), nosocomial infections, perinatal generalised disease; treatment: gentamicin, chloramphenicol; also susceptible to ciprofloxacin (MIC ≤ 0.06 mg/L), norfloxacin (≤ 0.06 mg/L), meropenem (0.06 mg/L), enoxacin (0.13 mg/L), imipenem (0.5 mg/L), cefperazone, mezlocillin, piperacillin, carbenicillin, gentamicin, tobramycin

Klebsiella: Gram negative rods, capsulated, nonmotile; indole negative (except *K.oxytoca*); lysine positive on lysine iron agar slant; gas, but not hydrogen sulphide, produced on acid TSI agar slant; present in vegetation, soil, sometimes faeces;

normal flora of vagina (2%); pathogenic when host resistance lowered; causes ankylosing spondylitis, 4-8% of bacteraemia and septicemia, asymptomatic bacteriuria, acute cystitis, acute empyema, human bite and clenched fist infections, chronic eye infections, neonatal and post-neonatal pyogenic meningitis, mycotic aneurism, 8% of nosocomial infections (15% of Gram negative bacilli), osteomyelitis and osteochondritis, otitis, peritonitis, pneumonia, pulmonary abscess, localised skin lesions in septicemia and endocarditis, septic arthritis, surgical wound infections (5% of total; summer peak), thrombophlebitis; extracellular; growth stimulated by excess iron; K (capsular) antigens, O antigens and endotoxin virulence factors; primary bodily defence mechanisms phagocytes (+), alternative complement (+), leucocyte bactericidal function (+), immune adherence (phagocytosis) (+++); susceptible to amoxycillin-clavulanate (in Australia, 10% acquired resistance in hospitals and 5% in private laboratories), piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, cafaclor, cefuroxime, cefotaxime and ceftriaxone (in Australia, 5% resistance in hospitals and 0.9% in private laboratories), cefepime, cefpirome, ceftazidime (MIC 1 mg/L), cefotetan, cefoxitin, norfloxacin (UTI only; 4% resistance in Australia), gentamicin (in Australia, 8% resistance in hospitals and 5% in private laboratories), tobramycin, ciprofloxacin (4% resistance in Australia), pefloxacin (0.5 mg/L), gatifloxacin, moxifloxacin, colistin (0.5 mg/L), imipenem (in Australia, 0.8% resistance in hospitals, none so far in private laboratories), meropenem, ceftizoxime (97% at < 1 mg/L), moxalactam, (< 1 mg/L), amifloxacin (1 mg/L), lomefloxacin (1 mg/L), neomycin (1 mg/L), amikacin, aztreonam, chloramphenicol; variably susceptible to doxycycline, tetracycline, minocycline; 98% intrinsic resistance (due to β-lactamase) to ampicillin, amoxycillin, azlocillin, carbenicillin, ticarcillin, piperacillin (possibly all resistant in clinical practice); in Australia, 12% acquired resistance to cotrimoxazole, 12% in hospitals and 16% in private laboratories to trimethoprim, 19% acquired resistance to cephalothin, cephazolin and cephalexin in hospitals and 10% in private laboratories

K.granulomatis: pleomorphic rods; cells exhibit single or bipolar condensation of chromatin or 'safety pin' forms; capsule present; exudate from infected tissues, when stained by Wright's stain or Giemsa stain, demonstrate characteristic intracellular blue to purple pleomorphic rods surrounded by pink capsules in cytoplasm of large mononuclear phagocytes; cultured in vitro on special egg yolk-containing media; optimum temperature 37°C; pathogenic for humans, causing granuloma inguinale (ulcerative lesions; commoner in tropics; sexually transmitted), hepatic granuloma; treatment: streptomycin, tetracycline, doxycycline, cotrimoxazole, chloramphenicol, gentamicin, erythromycin

K.oxytoca: isolated from water and human wounds and respiratory and urinary infections; also causes cholangitis and cholecystitis, malignant otitis externa (rare), pyomyositis (uncommon); susceptible to meropenem (MIC 0.06 mg/L), ceftazidime (98% of hospital isolates), ceftriaxone (94% of hospital isolates), cefpiramide (0.1-0.5 mg/L), aztreonam (94% of hospital isolates), cefpirome (0.12-0.25 mg/L), moxalactam (0.12-0.25 mg/L), carumonam (0.12-0.5 mg/L), cefmenoxime (0.12-1 mg/L), ceftizoxime (0.12-1 mg/L), pefloxacin (0.25-0.5 mg/L), foramidocillin (0.25-0.5 mg/L), ceftazidime (0.25-0.5 mg/L), cefbuperazone (0.25-1mg/L), ciprofloxacin (100%), ofloxacin (100%), imipenem (100%), enoxacin (99%), gentamicin (98% of hospital isolates), tobramycin (100%), cotrimoxazole (100%), cefotaxime (96% of hospital isolates)

K.pneumoniae: lysine decarboxylase, urease, VP, malonate, glucose (with gas) and lactose positive; ornithine decarboxylase and H_2S negative; methyl red variable; nonmotile, gas produced; causes acute empyema, cholangitis and cholecystitis, endotoxinemia, acute epididymitis and epididymoorchitis, neonatal necrotising enterocolitis, perianal and perirectal abscess and cellulitis in patients with malignant disease, perinatal generalised disease, peritonitis, primary and secondary pneumonia, pulmonary abscess, rhabdomyolysis, septicemia in haemodialysis, infections in abnormal host, systemic infections in granulocytopenia, hepatic abscess and endophthalmitis in diabetics; adherence to nasal mucosa ±; polysaccharide resists phagocytosis (unless antibody present) and digestion; capsular K antigens and cell wall O antigens associated with invasiveness; diagnosis: counterimmunoelectrophoresis, culture; treatment: cefotaxime (6% resistance (due to β-lactamase) in Australia), gentamicin (11% resistance in Australia), amikacin, ceftazidime (6% resistance in hospitals), ciprofloxacin (4% resistance in Australia and USA), aztreonam (7% resistance in hospitals), chloramphenicol; also susceptible to meropenem (0.06 mg/L), ceftizoxime (≤ 0.12 mg/L), cefmenoxime (≤ 0.12 mg/L), cefpirome (≤ 0.12 mg/L), carumonam (0.12-0.25 mg/L), cefixime (≤ 0.25 mg/L), ofloxacin (0.25 mg/L), cefbuperazone (0.25-0.5 mg/L), enoxacin (97% at 0.5 mg/L), oxolinic acid (0.5 mg/L), cefaclor (0.5 mg/L), pefloxacin (0.5 mg/L), foramidocillin (0.5-1 mg/L), rosoxacin (0.8 mg/L), imipenem (0.4% resistance in Australia), moxalactam, ceftriaxone (6% resistance in Australia), levofloxacin (3% resistance in USA); resistant to carbenicillin, azlocillin, piperacillin; in Australia, 15% resistance to cotrimoxazole (10% in USA), 21% resistance (due to β-lactamase) to cephalothin (13% in USA), cephazolin, cephalexin, 11% resistance to amoxycillin-clavulanate (9% in USA), 7% resistance to tobramycin (15% in hospital isolates), 7% resistance to norfloxacin (5% in USA)

K.pneumoniae subsp ozaenae: urease, VP and malonate negative; causes infections in abnormal host; susceptible to meropenem (MIC 0.25 mg/L)

K.pneumoniae subsp rhinoscleromatis: malonate, glucose and lactose positive; urease, VP, indole and H_2S negative; nonmotile, gas not produced; causes rhinoscleroma, infections in abnormal host

Kluyvera ascorbata: isolated from water and human wounds; infrequently causes peritonitis

Morganella morganii: phenylalanine deaminase, ornithine decarboxylase, indole, glucose and urease positive; citrate, H_2S and lactose negative; motility and gas from glucose variable; not spreading on blood agar; causes bacteraemia and septicemia in neutropenics and long term care, infections in abnormal host, nosocomial infections, typhlitis, urinary tract

infections (chronic bacteriuria); susceptible to ciprofloxacin (100% at 0.03 mg/L), gatifloxacin, moxifloxacin, carumonam (0.12 mg/L), ofloxacin (100% at 0.25 mg/L), lomefloxacin (0.5 mg/L), norfloxacin (100% at 0.5 mg/L), enoxacin (0.5 mg/L), pefloxacin (0.5 mg/L), aztreonam, chloramphenicol, cotrimoxazole (100% at 1 mg/L), gentamicin (100%), amikacin, trimethoprim, tobramycin (100%); 98% resistance (due to β-lactamase) to amoxycillin, ampicillin, amoxycillin-clavulanate, cephalothin, cephazolin, cefaclor, cefuroxime, cephalexin (possibly all resistant in clinical practice); possesses an inducible Class I chromosomal β-lactamase and should be considered resistant to all cephalosporins, penicillins, cephamycins and aztreonam but may be susceptible to imipenem, meropenem

Pantoea

Enterobacter agglomerans: rhamnose positive (may be delayed); indole, methyl red, VP, Simmon's citrate, urease, KCN, motility, phenylalanine deaminase, gas from glucose, lactose, sucrose, dulcitol, inositol and raffinose variable; causes endotoxinemia, infusion infection; susceptible to ceftriaxone (MIC 0.03 mg/L), cotrimoxazole (≤ 0.06-0.12 mg/L), meropenem (0.13 mg/L), moxalactam (0.25 mg/L), cefotaxime (0.25-0.5 mg/L), imipenem (0.5 mg/L), gentamicin (0.5 mg/L), ciprofloxacin (100%), enoxacin (94%), norfloxacin (94%)

Plesiomonas: inositol and ornithine decarboxylase positive; mannitol and gelatinase negative; O/129 susceptible; one case of postoperative pancreatic abscess; susceptible to ciprofloxacin (< 5% resistance in Australia), norfloxacin (MIC 0.06-0.5 mg/L), enoxacin (0.125-0.5 mg/L), nalidixic acid (0.5 mg/L)

P.shigelloides: straight, variable length rods; asporogenous; motile by a tuft of polar flagella; facultatively anaerobic (both respiratory and fermentative type of metabolism); growth at 37°C; NaCl not required; colonies greyish, shiny, opaque, slightly raised centre, smooth entire edge, no brown pigment; not β-haemolytic on blood agar; grows on MacConkey and SS; lysine decarboxylase, ornithine decarboxylase, arginine dihydrolase, oxidase, catalase, indole, nitrate (no gas), and methyl red positive; VP, Simmon's citrate and gelatine negative; acid from glucose (no gas), maltose, lactose and inositol but not mannitol, sorbitol, rhamnose, melibiose, amygdalin, arabinose; negative reactions for urease, amylase, lipase and proteinase; most strains susceptible to O/129; occurs in fish and other aquatic animals and in a variety of mammals; isolated from human stool, CSF, knee, wound, urine, abscess, blood, leg and paracentesis fluid; causes cholecystitis, gastroenteritis (occasional outbreaks and sporadic cases, chiefly in tropical areas), infections in abnormal host, osteomyelitis, meningitis, proctitis with fatal septicemia, bacteraemia secondary to cellulitis; susceptible to ciprofloxacin (MIC 0.008 mg/L), ofloxacin (0.015 mg/L), meropenem (≤ 0.06 mg/L), pefloxacin (0.06 mg/L), fleroxacin (0.06-0.25 mg/L), imipenem (100%)

Proteus: Gram negative rods, motile; urease and phenylalanine deaminase positive; lysine decarboxylase negative; normal flora of colon; common in soil, faeces; occasionally pathogenic; causes 1-3% of bacteraemia and septicemia, acute cystitis, acute pyelonephritis, asymptomatic bacteriuria, chronic bacteriuria (endogenous; associated with infected bladder or renal stones, bladder diverticulum, renal abscess, indwelling catheter), urethritis, enterotoxaemia and gastroenteritis (rare), chronic eye infections, foot and leg sores in diabetics, Fournier's gangrene of scrotum, human bite and clenched fist infections, intraabdominal abscess, local and generalised sepsis, mastitis and breast abscess, neonatal and postneonatal purulent meningitis, acute empyema, mycotic aneurism, osteomyelitis and osteochondritis, 2% of otitis externa, septic arthritis, 7% of surgical wound infections, other wound infections, 7% of nosocomial infection, 8% of vascular graft infections; extracellular; growth stimulated by excess iron; treatment: gentamicin (100% susceptible), chloramphenicol; also susceptible to ciprofloxacin (MIC 0.03-0.12 mg/L), ofloxacin (0.12-0.25 mg/L), lomefloxacin (0.25 mg/L), norfloxacin (0.5 mg/L), enoxacin (0.5 mg/L), ceftozoxime, moxalactam, mezlocillin, carbenicillin, tobramycin (100%), amikacin, aztreonam (100%)

P.mirabilis: ornithine decarboxylase, citrate (may be delayed), H_2S, glucose (with gas), urease, phenylalanine deaminase and gelatine positive; indole and lactose negative; VP, sucrose and salicin variable; spreading on blood agar; normal flora of cervix (10%); causes asymptomatic bacteriuria, acute empyema, endocarditis, endophthalmitis, malignant otitis externa (rare), 3% of nosocomial infections (5% of Gram negative bacilli), perianal and perirectal abscess and cellulitis in patients with malignant disease, infections in abnormal host; susceptible to amoxycillin-clavulanate (9% resistance due to β-lactamase in Australia, 4% in USA), piperacillin-tazobactam, ticarcillin-clavulanate, cefaclor, cefmenoxime (MIC ≤ 0.01 mg/L), cefpirome (≤ 0.01 mg/L), aztreonam (100%), carumonam (≤ 0.01 mg/L), meropenem (0.13 mg/L), ciprofloxacin (0.4% resistance in Australia, 14% in USA), ofloxacin (100% at 0.25 mg/L), norfloxacin (0.4% resistance in Australia, 15% in USA), gatifloxacin, moxifloxacin, cefixime (≤ 0.25 mg/L), amifloxacin (0.25 mg/L), foramidocillin (0.25-0.5 mg/L), enoxacin (0.25-0.5 mg/L), carbenicillin (≤ 0.5 mg/L), pefloxacin (0.5-1 mg/L), cefotetan/cefotxitin (0.5-1 mg/L), cefotaxime/ceftriaxone (0.5% resistance in Australia), cefepime, ceftizoxime (100% at < 1 mg/L), mezlocillin (< 1 mg/L), apalcillin (< 1 mg/L), moxalactam (1 mg/L), cefuroxime (1 mg/L), gentamicin (2% resistance in Australia), ceftazidime (100%), tobramycin (3% resistance in hospitals in Australia), amikacin, levofloxacin (13% resistance in USA), chloramphenicol, rifampicin/rifabutin; 95% intrinsic resistance to nitrofurantoin (98% in USA) and 98% to tetracycline (possibly all resistant in clinical practice); in Australia, 18% resistance (due to β-lactamase) to amoxycillin/ampicillin (15% in USA), ticarcillin, piperacillin, azlocillin, 18% resistance to cotrimoxazole (16% in USA), 28% resistance to trimethoprim, 10% resistance (due to β-lactamase) to cephalothin (13% in USA), cephazolin and cephalexin, 18% resistance to imipenem

P.vulgaris: phenylalanine deaminase, gelatine, glucose, sucrose, indole, H_2S and urease positive; ornithine decarboxylase and lactose negative; gas from glucose and citrate variable; spreading on blood agar; causes asymptomatic bacteriuria

(frequently extraneous), infections in abnormal host; susceptible to ciprofloxacin (100% at 0.06 mg/L), gatifloxacin, moxifloxacin, carumonam (≤ 0.12 mg/L), pefloxacin (0.25 mg/L), cotrimoxazole (100% at 0.5 mg/L), norfloxacin (100%), enoxacin (100%), trimethoprim, gentamicin (100%), amikacin, tobramycin (100%), aztreonam, chloramphenicol; 96% intrinsic resistance (due to β-lactamase) to amoxycillin and ampicillin, 92% to amoxycillin-clavulanate, 97% to cephalothin, cephazolin, cefaclor, cefuroxime, and cephalexin (possibly all resistant in clinical practice); possesses an inducible Class I chromosomal β-lactamase and should be considered resistant to all cephalosporins, penicillins, cephamycins and aztreonam but may be susceptible to imipenem, meropenem; commonly resistant to tetracyclines

Providencia: phenylalanine deaminase and indole positive; normal inhabitant of intestinal tract; causes 0.1% of bacteraemia and septicemia, nosocomial infections, osteomyelitis, 20% of thrombophlebitis, urinary tract infections (chronic bacteriuria); susceptible to pefloxacin (MIC 0.25 mg/L), ciprofloxacin (0.5 mg/L), gatifloxacin, moxifloxacin, ofloxacin (1 mg/L), lomefloxacin (1 mg/L), aztreonam, chloramphenicol, cotrimoxazole, trimethoprim, gentamicin, tobramycin, amikacin; 96% intrinsic resistance (due to β-lactamase) to amoxycillin and ampicillin, 92% to amoxycillin-clavulanate, 97% to cephalothin, cephazolin and cephalexin (possibly all resistant in clinical practice); possesses an inducible Class I chromosomal β-lactamase and should be considered resistant to all cephalosporins, penicillins, cephamycins and aztreonam but may be susceptible to imipenem, meropenem; usually resistant to tetracycline

P.alcalifaciens: glucose, phenylalanine and adonitol positive; ornithine decarboxylase, inositol, sorbitol, lactose, H_2S and urease negative; sucrose and gas from glucose variable; motile; causes infections in abnormal host; susceptible to meropenem (MIC 0.13 mg/L)

P.rettgeri: phenylalanine deaminase, urease, citrate, indole, and glucose positive; ornithine decarboxylase, H_2S and lactose negative; sucrose, mannitol, salicin, sorbitol and rhamnose variable; gas usually not produced; causes 0.5-1% of bacteraemia and septicemia in long term care patients, infections in abnormal host; susceptible to ceftriaxone (MIC 0.008 mg/L), aztreonam (0.125 mg/L), cefixime (≤ 0.25 mg/L), meropenem (MIC 0.25 mg/L), pefloxacin (0.5 mg/L), cefuroxime (1 mg/L), ciprofloxacin (100%), enoxacin (100%), norfloxacin (93%), ofloxacin (92%), cefoperazone, ceftizoxime

P.stuartii: indole, phenylalanine deaminase, inositol and sucrose (may be delayed) positive; urease, ornithine decarboxylase and gas from glucose negative; adonitol and mannitol variable; causes 13% of bacteraemia and septicemia in long term care patients, chronic bacteriuria in indwelling catheter; susceptible to cefotaxime (MIC 0.06-0.5 mg/L), ceftizoxime (0.06-1 mg/L), cefmenoxime (0.06-1 mg/L), ceftriaxone (0.06-1 mg/L), ceftazidime (0.06-1 mg/L), cefpirome (0.06-1 mg/L), aztreonam (< 0.12 mg/L), carumonam (< 0.12 mg/L), cefixime (≤ 0.25 mg/L), meropenem (0.5 mg/L), moxalactam (0.5-1 mg/L), imipenem (100%); resistant to amoxycillin-clavulanate

Rahnella aquatilis: isolated from water and human wounds

Salmonella: Gram negative rods; motile; glucose, mannitol, sorbitol, arabinose (usually), rhamnose, arginine dihydrolase (may be delayed) and ornithine decarboxylase positive; indole, lactose, sucrose, salicin, adonitol, urea, malonate, gelatine and KCN negative; dulcitol, inositol and Simmon's citrate variable; aerogenic (gas produced on acid, alkaline or neutral TSI agar slant; except *S.typhi*); H_2S produced on TSI and LIA slants (except some strains of '*S.paratyphi A*'); lysine debarboxylase positive on LIA slant (except '*S.parathyphi A*'); causes enteric fever (typhoid, paratyphoid; continued fever, often without significant diarrhoea), gastroenteritis (food poisoning, salmonellosis), acute diarrhoea (0-25% of traveller's, 0-3% of nosocomial; 52% of enteric pathogen isolates) and/or vomiting, 13% of waterborne disease outbreaks (source animal and human faeces; survival time 12 h - 5 d), reactive arthritis, bacteremia and septicemia, endocarditis (AIDS patients, oncology patients, elderly with previous valvular heart disease), asymptomatic bacteriuria in renal transplant recipients, brain and epidural abscess (uncommon), cellulitis (in renal transplant recipients), acute epididymitis and epididymoorchitis, 18-66% of mycotic aneurism, neonatal and postneonatal purulent meningitis, orchitis (in renal transplant recipients), osteomyelitis and osteochondritis (associated with hemoglobinopathies, particularly sickle cell disease; more likely in patients with lymphoma or connective tissue disorders), pneumonia (in renal transplant recipients), acute pyelonephritis (in renal transplant recipients), septic arthritis (< 20 y; related to sickle cell disease), acute sinusitis (in renal transplant recipients), local and generalised sepsis (in renal transplant recipients), splenic abscess, infections in abnormal host (infusion infection, T lymphocyte dysfunction); ≈ 2100 serotypes; primarily parasite of animals (pythons to elephants), great tendency to colonise domestic animals (pigs and poultry commonly affected); human disease usually follows consumption of contaminated meat (poultry, pork, ham, beef, meat pies, sausages) or eggs; also milk, unpasteurised orange juice; contaminates raw materials or food after cooking and is subsequently allowed to multiply; most species extracellular; causes profuse watery diarrhoea or dysentery (abdominal cramps, tenesmus, usually blood in stool); attaches to and penetrates epithelium of ileum, causing disease by killing epithelial cells (invasive infection with possible toxin involvement) and inducing diarrhoea; growth stimulated by excess iron; in certain species, infection is generally confined to epithelial surface of intestinal tract; certain species also invade subepithelial tissues of small bowel and colon, penetrating into submucosa and causing disease by inflammation of the lamina propria; disease-producing dose for most serotypes 10^5-10^8 organisms; most serotypes transmitted by food or water; Vi antigen, O antigens and endotoxin virulence factors; M antigens also present; immunity cell-mediated (delayed type hypersensitivity activated macrophages +++), bactericidal activity +, immune adherence (phagocytosis) ++; serotyped on basis of antigenic polysaccharides (O antigens) consisting of repeating units containing 3-5 sugars each in outermost regions

of lipopolysaccharide; diagnosis: Widal agglutination (significant titre ≥ 1:80), indirect haemagglutination (4-fold rise in titre indicates active infection), ELISA, stool and blood cultures (preferred method), Wellcolex colour Salmonella test on culture in selenite broth (sensitivity 97.6%, specificity 99.7%); susceptible to cotrimoxazole (MIC 0.032-0.5 mg/L), chloramphenicol, cefotaxime (0.003-0.5 mg/L), ceftriaxone (0.01-0.2 mg/L), cefepime, ampicillin, amoxycillin, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, ofloxacin (0.032-0.06 mg/L), tetracycline, meropenem (≤ 0.06 mg/L), ceftazidime (0.06-0.5 mg/L), cefmenoxime (≤ 0.12 mg/L), cefuroxime, aztreonam (≤ 0.12 mg/L), carumonan (≤ 0.12 mg/L), ciprofloxacin (< 5% resistance in Australia), gatifloxacin, moxifloxacin, cefpirome (0.12 mg/L), pefloxacin (0.25 mg/L), fleroxacin (0.25 mg/L), norfloxacin (100% at 0.5 mg/L), enoxacin (100% at 0.5 mg/L), imipenem (100% at < 1 mg/L), amoxycillin-clavulanate, trimethoprim, nalidixic acid, azithromycin

S.choleraesuis: arabinose negative; causes enteric fever, endocarditis (26% of *Salmonella* isolates), septic arthritis; 4% of *Salmonella* blood isolates, 1% of *Salmonella* CSF isolates; main host swine; treatment: chloramphenicol

S.enterica

Subsp *S.enterica I*

***S.anatum*:** 6-9% of total *Salmonella* isolates (70% from animal, 13% from human), 2% of urine isolates, 1% of stool, 0.5% of CSF; transmitted by non-fat powdered milk, unpasteurised orange juice

***S.blockley*:** 2% of *Salmonella* stool isolates, 1% of *Salmonella* CSF isolates, 1% of *Salmonella* urine isolates, 0.5% of *Salmonella* blood isolates; causes rhabdomyolysis

***S.derby*:** 10-13% of total *Salmonella* isolates (69-81% from animal products), 2% of CSF isolates, 2% of urine, 2% of stool, 0.6% of blood

***S.dublin*:** causes 40% of gastroenteritis due to pasteurised milk, 34% of cases due to raw milk; 4% of *Salmonella* blood isolates, 2% of *Salmonella* CSF isolates; 44% of human isolates obtained from stool, 37% from blood, 6% from urine, 2% from gallbladder, 1% from wound; 10% of cattle infected

serovar aberdeen: 0.3% of *Salmonella* CSF isolates

serovar adelaide: 1-3% of *Salmonella* isolates (29-62% from animal products)

serovar agona: 5% of total *Salmonella* isolates, 3% of poultry isolates, 3% of CSF isolates, 3% of urine, 3% of stool, 1% of blood; transmitted by non-fat powdered milk, raw milk, other food and water, contact, fomites; disease-producing dose 10^2 organisms

serovar bareilly: 1% of total *Salmonella* isolates (15% from animals), 0.8% of CSF isolates

serovar berta: 0.5% of *Salmonella* CSF isolates

serovar bovis-morbificans: 2-5% of total *Salmonella* isolates (44-75% from animal products), 0.3% of CSF isolates

serovar braenderup: outbreak of salmonellosis due to contaminated tomates

serovar brandenburg: 0.5% of *Salmonella* CSF isolates

serovar bredeney: 3% of total *Salmonella* isolates (69% from animals), 0.8% of CSF isolates

serovar cerro: 1% of total *Salmonella* isolates (96% from animal products, especially raw milk)

serovar chester: 2-5% of total *Salmonella* isolates (35-57% from humans), 3% of clinical isolates, 0.8% of CSF isolates

serovar copenhagen: causes 20% of gastroenteritis due to pasteurised milk

serovar cubana: 0.3% of *Salmonella* CSF isolates; transmitted by non-fat powdered milk

serovar eastbourne: disease-producing dose 10^2 organisms; transmitted by food, water, contact, fomites

serovar havana: 3-4% of total *Salmonella* isolates (42-48% from animal products)

serovar heidelberg: causes gastroenteritis; 7% of total *Salmonella* isolates, 16% of CSF isolates, 9% of blood, 8% of urine, 7% of stool; disease-producing dose 10^2 organisms; transmitted by food, water, contact, fomites

serovar java: 0.5% of *Salmonella* CSF isolates

serovar javiana: 2% of *Salmonella* urine isolates, 2% of *Salmonella* stool isolates, 1% of *Salmonella* CSF isolates, 0.7% of *Salmonella* blood isolates

serovar johannesburg: 1% of total *Salmonella* isolates (≈ 100% from animal products), 0.8% of CSF isolates

serovar kentucky: 0.3% of *Salmonella* CSF isolates; transmitted by raw milk

serovar kottbus: 2% of total *Salmonella* isolates (94% from animal products), 0.5% of CSF isolates

serovar lille: transmitted by raw milk

serovar manhattan: 2% of *Salmonella* urine isolates, 1% of *Salmonella* stool isolates, 0.5% of *Salmonella* CSF isolates

serovar marina: diarrhoea associated with pet iguanas

serovar mbdantaka: infectious dose in peanut butter < 5 organisms

serovar meleagridis: transmitted by raw milk

serovar miami: causes gastroenteritis

serovar minnesota: 0.5% of *Salmonella* CSF isolates; inhibits phagocytic microbicidal activity by resistance to granule substance

serovar newington: 0.3% of *Salmonella* CSF isolates; transmitted by raw milk

serovar ohio: 0.5% of *Salmonella* isolates from poultry

serovar onderstepoort: 1-2% of total *Salmonella* isolates (92-95% from animal products)
serovar panama: 4% of *Salmonella* CSF isolates, 1% of *Salmonella* stool isolates, 1% of *Salmonella* blood isolates, 1% of *Salmonella* urine isolates
serovar paratyphi B: 1% of blood isolates, causes hepatic granuloma
serovaar paratyphi C: causes endocarditis, septic arthritis
serovar pensacola: 0.3% of *Salmonella* CSF isolates
serovar poona: 1% of CSF isolates; cantaloupe
serovar reading: 0.3% of *Salmonella* CSF isolates
serovar saint-paul: causes salmonellosis; 3% of total *Salmonella* isolates, 5% of clinical isolates, 6% of CSF isolates, 4% of stool, 4% of urine, 3% of blood; transmitted by raw milk
serovar san-diego: 1% of *Salmonella* CSF isolates
serovar schottmuelleri: causes enteric fever
serovar schwarzengrund: 0.7% of *Salmonella* blood isolates
serovar sendai: main host man
serovar singapore: 5-10% of *Salmonella* isolates (32-34% from animals)
serovar sofia: 90% of *Salmonella* isolates from poultry
serovar stanley: 0.3% of *Salmonella* CSF isolates; transmitted by peanuts (infectious dose up to 200 organisms)
serovar tennessee: transmitted by non-fat milk
serovar urbana: 1% of *Salmonella* CSF isolates
serovar welikade: 1% of *Salmonella* isolates (92% from animal products)
serovar weltevreden: 0.3% of *Salmonella* CSF isolates
serovar wien: disease-producing dose 10^2 organisms; transmitted by food, water, contact, fomites
serovar worthington: transmitted by raw milk
***S.gallinarum*:** main host fowl
***S.hadar*:** 46% of gastroenteritis cases transmitted by turkey; 2-10% of *Salmonella* strains isolated from chickens
***S.infantis*:** 5% of total *Salmonella* isolates, 6% of urine isolates, 3% of blood, 2% of CSF
***S.montevideo*:** 2% of total *Salmonella* isolates, 2% of CSF isolates, 2% of urine, 2% of stool, 1% of blood; transmitted by raw milk
***S.muenchen*:** causes salmonellosis; transmitted by poultry, cattle, swine, marijuana, unpasteurised orange juice; 2-3% of total *Salmonella* isolates (58-62% from animal products)
***S.muenster*:** causes gastroenteritis; 0.3% of *Salmonella* CSF isolates; transmitted by undercooked turkey
***S.newport*:** causes 20% of gastroenteritis due to pasteurised milk; outbreaks due to contaminated tomatoes; 1-6% of total *Salmonella* isolates (80% from animals), 4% of clinical isolates, 7% of stool isolates, 5% of urine, 4% of CSF, 2% of blood; disease-producing dose 10^2 organisms; transmitted by food, water, contact, fomites
***S.oranienburg*:** causes gastroenteritis, soft tissue and cartilage infection; 2-3% of total *Salmonella* isolates (56-75% from animal products), 2% of CSF isolates, 2% of blood, 2% of urine, 2% of stool
S.paratyphi A: causes enteric fever; 2% of *Salmonella* blood isolates, 0.3% of CSF isolates; attaches to and penetrates epithelium of small intestine and invades subepithelial tissues; facultative intracellular; main host man; treatment: chloramphenicol, ciprofloxacin, amoxycillin, ceftriaxone, ofloxacin
***S.thompson*:** 2% of *Salmonella* blood isolates, 2% of *Salmonella* urine isolates, 2% of *Salmonella* blood isolates, 1% of *Salmonella* CSF isolates
***S.virchow*:** 6% of *Salmonella* clinical isolates
Subsp enterica subsp arizonae: H_2S, gelatine (delayed), lysine decarboxylase, arginine dihydrolase (may be delayed), ornithine decarboxylase, malonate, lactose, mannitol, sorbitol, arabinose, and rhamnose positive; gas from glucose; KCN and salicin negative
***S.enteritidis*:** 6% of *Salmonella* isolates (10% of blood, 9% of CSF, 7% of stool, 7% of urine); causes 13% of *Salmonella* endocarditis; main species transmitted by eggs; susceptible to fleroxacin (MIC 0.5 mg/L)
S.typhi: natural host man; invasive; causes enteric fever (typhoid fever; 31 M cases with 581 000 deaths (94% < 5 y) globally annually), septic arthritis, bacteraemia and septicemia, bone marrow infection, adult hepatitis, hepatic granuloma, osteomyelitis, pancreatic abscess, rhabdomyolysis; 2% of total *Salmonella* isolates, 23% of blood isolates, 6% of CSF, 5% of urine, 2% of stool; oral disease-producing dose in man 10^4-10^6 bacteria; bacterial adhesin attaches to mannose-like receptor on epithelial cell of small intestine, invades subepithelial tissues, replicates in intestinal lymphoid tissue, liver, biliary tract, subsequently spreads through body; biliary excretion of bacteria into intestine; inhibits phagocytic chemotaxis and oxidative burst; Vi antigen (poly-N-acetyl-D-galactosaminouronic acid) resists phagocytosis (unless antibody present) and killing (associated with invasiveness); O antigens (polysaccharide-protein-phospholipid complex) inhibit phagocytosis, inhibit complement, modify fibrinogen and potentiate effects of epinephrine; facultative intracellular; recovery from primary infection due to cell-mediated immunity; antibodies to cells containing O antigen confer specific immunity; persists in gall bladder and

urinary tract (infectious, intermittent shedding in urine and faeces); transmitted by food and water; treatment: chloramphenicol, cotrimoxazole, ciprofloxacin (MIC 0.02-0.1 mg/L), amoxycillin, ceftriaxone, ofloxacin (0.1 mg/L), amoxycillin-clavulanate; also susceptible to meropenem (≤ 0.06 mg/L) norfloxacin (0.2 mg/L), fleroxacin (0.25 mg/L), rosoxacin (0.4 mg/L)

***S.typhimurium*:** causes 20% of gastroenteritis due to pasteurised milk (also transmitted by non-fat powdered milk, raw milk, tomatoes, other food, water, contact, fomites), 21% of *Salmonella* endocarditis, septic arthritis in renal transplant recipients; most commonly isolated *Salmonella* (35-38% of total isolates (47-60% from animals), 3% of poultry isolates, 28% of clinical isolates, 30% of stool, 23% of urine, 22% of CSF, 20% of blood); multiple sources, including eggs, Turkish helva, wild birds; disease-producing dose from 10^2 organisms in halva to > 20 000 organisms in rice dish; mean doubling time 30 minutes in vitro, 5-12 h in mouse spleen; inhibits phagocytic microbicidal activity by resistance to granule (lysosomal enzymes); susceptible to macrophage colony stimulatory factor-activated macrophages; interferon γ, interferon β, interleukin 1, granulocyte macrophage colony stimulatory factor, tissue necrosis factor also induce antimicrobial activity; treatment: chloramphenicol

Serratia: gelatine (may be delayed), lysine decarboxylase (may be delayed), mannitol, sucrose, salicin (may be delayed) positive; widely distributed opportunistic pathogen; causes 2% of bacteraemia and septicemia, neonatal meningitis, osteomyelitis and osteochrondritis (spine, sacroiliac joint, sternoclavicular joint, symphysis pubis, as well as usual large joints, in drug addicts), primary and secondary pneumonia, 2% of nosocomial infection, systemic infections in microbicidal abnormality; inhibits phagocyte chemotaxis; K antigens, O antigens and endotoxin virulence factors; major host defence mechanisms phagocytes (+), alternative complement (+), bactericidal activity (+), immune adherence (phagocytosis) (+++); susceptible to cefotaxime, ceftriaxone, cefepime, cefpirome, ceftazidime, foramidocillin (MIC 0.25-0.5 mg/L), ofloxacin (0.5 mg/L), lomefloxacin (0.5 mg/L), enoxacin (95% at 0.5 mg/L), pefloxacin (1 mg/L), imipenem (100%), meropenem, ceftizoxime (96%), norfloxacin (93% at 0.5 mg/L), cefoperazone, moxalactam, mezlocillin, amikacin, usually susceptible to cotrimoxazole, trimethoprim, gentamicin, tobramycin, ciprofloxacin, gatifloxacin, moxifloxacin, aztreonam, ticarcillin, piperacillin, azlocillin, piperacillin-tazobactam, ticarcillin-clavulanate; 96% intrinsic resistance (due to β-lactamase) to amoxycillin and ampicillin, 92% to amoxycillin-clavulanate, 97% to cephalothin, cephazolin and cephalexin (possibly all resistant in clinical practice)

S.liquefaciens: inositol (may be delayed), sorbitol, arabinose, raffinose, ornithine decarboxylase, gelatine and lysine decarboxylase positive; mucate negative; methyl red, VP, gas from glucose, lactose and urease variable; causes infections in abnormal host (infusion infections); susceptible to imipenem (100%), meropenem (MIC 0.13 mg/L)

S.marcescens: VP, gelatine (may be delayed), sorbitol, ornithine decarboxylase, glucose (with gas) and sucrose positive; mannose, rhamnose, lactose, H_2S, indole and arabinose negative; motile; water-borne; causes variety of infections (especially urinary and respiratory tract infections (including acute empyema) and septicemia (sometimes with localised skin lesions)), chiefly in abnormal host (interrupted integument) and hospital patients, also perinatal generalised disease, psoas abscess, rare pyomyositis; extracellular; primary bodily defence mechanism leucocyte bactericidal function; treatment: gentamicin (100% susceptible), chloramphenicol, tobramycin; also susceptible to oxolinic acid (0.25 mg/L), enoxacin (0.25 mg/L), meropenem (0.25 mg/L), rosoxacin (0.4 mg/L), amifloxacin (0.5 mg/L), norfloxacin (0.8 mg/L), ciprofloxacin (100% at 1 mg/L), pefloxacin (1 mg/L), imipenem (100%), piperacillin/tazobactam (100%); resistant to tetracycline, nitrofurantoin; possesses an inducible Class I chromosomal β-lactamase and should be considered resistant to all cephalosporins, penicillins, cephamycins and aztreonam but may be susceptible to imipenem

S.rubidaea: methyl red, VP, gelatine (may be delayed), arabinose, raffinose, lactose, adonitol (may be delayed) and inositol positive; ornithine decarboxylase and sorbitol negative; rhamnose, KCN, motility, malonate, gas from glucose and urease variable; isolated from water and human wounds; causes infections in abnormal host

Shigella: Gram negative rods; nonmotile; usually anaerogenic; glucose positive; lysine, oxidase, H_2S, citrate, sucrose, salicin, KCN, usually lactose negative; mannitol, dulcitol, sorbitol, arabinose, raffinose, rhamnose and indole variable; Kligler iron agar alkaline/acid; TSI agar slant acid, alkaline or neutral, with no gas (except some strains in a few serotypes) and no hydrogen sulphide; obligate parasite of man; local invasion only; causes profuse watery diarrhoea (no blood in stool), bacillary dysentery (303 M cases with 654 000 deaths (85% in children < 5 y) globally annually; abdominal cramps, tenesmus, usually blood in stool), bacteraemia and septicemia associated with severe dysentery (especially caused by *S.dysenteriae* serotype 1; uncommonly in neutropenics), 25% of waterborne disease outbreaks (source animal and human faeces; survival time < 15 - > 70 d), reactive arthritis, ? Reiter syndrome, adult hepatitis, symbiotic gangrene, infections in abnormal host; 4% of enteric pathogen isolates; disease-producing dose 10^1-10^4; transmitted by food, water, contact, fomites; attack rate 33-73% in day care centres; initially localises in small bowel, later attaches to and penetrates epithelium of large intestine, replicates in intestinal epithelium of large intestine, causing disease by killing epithelial cells (exotoxin formed) and inducing diarrhoea by mucosal damage and inflammation; infection generally confined to epithelial surface of intestinal tract; growth stimulated by excess iron; susceptible to amikacin, gentamicin, tobramaycin, imipenem, meropenem, cotrimoxazole (MIC 0.016-0.5 mg/L), sulphadimidine, tetracycline, ciprofloxacin (< 5% resistance in Australia), gatifloxacin, moxifloxacin, ofloxacin (0.032-0.25 mg/L), norfloxacin (0.032-0.5 mg/L), fleroxacin (0.125 mg/L), enoxacin (0.25-0.5 mg/L), pefloxacin (0.06-

0.12 mg/L), aztreonam, cefotaxime (< 1 mg/L), ceftizoxime (< 1 mg/L), moxalactam (< 1 mg/L), ceftriaxone (< 1 mg/L), ceftazidime (< 1 mg/L), amoxycillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, cefuroxime, cefepime, cefpirome, cefotetan/cefoxitin, chloramphenicol, trimethoprim, nalidixic acid

S.boydii: mannitol positive; lactose, dulcitol and ornithine decarboxylase (except type 13) negative; indole variable; serologic subgroup A; types 1-15; causes 2-3% of shigellosis cases, dysentery; susceptible to fleroxacin (MIC 0.25 mg/L)

S.dysenteriae: mannitol and ornithine decarboxylase negative; serologic subgroup A; types 1-10; causes 1% of shigellosis cases, dysentery; oral disease-producing dose in man 10 bacteria; enterotoxin induces fluid loss from intestine, causing diarrhoea; neurotoxin induces vascular endothelial damage in brain, causing neurological disturbances; susceptible to norfloxacin (MIC 0.05 mg/L), fleroxacin ($\leq$ 0.06 mg/L), rosoxacin (0.2 mg/L)

S.flexneri: mannitol positive; lactose, dulcitol and ornithine decarboxylase negative; indole variable; some strains gas from glucose; serologic subgroup B; types 1-6; causes 29% of total shigellosis cases (46% due to types 2a and 3a; 58% of shigellosis cases on Indian reservations, 23% in general community, 7% in institutions), dysentery, rhabdomyolysis, splenic abscess (extremely rare); attaches to colonic epithelium; susceptible to meropenem (MIC 0.03 mg/L), fleroxacin (0.125 mg/L)

S.sonnei: mannitol, lactose (late), sucrose (late) and ornithine decarboxylase positive; sorbitol negative; serologic subgroup D; 1 type; causes 67% of shigellosis cases (93% of shigellosis in institutions, 74% in general community, 41% on Indian reservations; very mild infection), dysentery, rhabdomyolysis; susceptible to fleroxacin (MIC $\leq$ 0.06 mg/L), meropenem (0.06 mg/L)

Yersinia: Gram negative rods and ovals, bipolar staining; colonies < 1 mm on nutrient agar after 24 h at 37°C; growth on MacConkey, growth on SS variable; fermentative, nitrate reduced to nitrite; mannitol and arabinose positive; oxidase, lysine decarboxylase and arginine dihydrolase negative; ornithine decarboxylase variable; primarily animal parasite; causes yersinosis, reactive arthritis, enterocolitis (acute diarrhoea and/or vomiting, 4% of enteric pathogen isolates), erythema nodosum, mesenteric adenitis, plague; facultative intracellular; endotoxins present; susceptible to amoxycillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, ciprofloxacin (MIC 0.015-0.12 mg/L), gatifloxacin, moxifloxacin, norfloxacin, ceftriaxone (0.06-0.12 mg/L), cefotaxime (0.06-0.25 mg/L), ceftozoxime (0.06-0.25 mg/L), cefmenoxime (0.06-0.25 mg/L), cefpirome (0.06-0.25 mg/L), ceftazidime (0.12-0.5 mg/L), moxalactam (0.25 mg/L), cefepime, amikacin, gentamicn, tobramycin, carumonam (0.25-1 mg/L), imipenem (100%), meropenem, cotrimoxazole, doxycycline/tetracycline, minocycline, aztreonam, chloramphenicol, trimethoprim

Y.enterocolitica: motile at 20°C but not at 35°C; growth on MacConkey agar and Tergitol 7; ornithine decarboxylase, sorbitol, urease, salicin and D-galactosidase positive; grows at refrigeration temperatures; lysine decarboxylase, arginine dihydrolase, phenylalanine deaminase, gas from glucose, lactose, rhamnose, oxidase and Simmon's citrate negative; VP, inositol, indole and sucrose variable; cross-reacts serologically with *Brucella abortus*; isolated from water (source animal and human faeces; survival time days - weeks) and human infections; 86% of infections gastroenteritis (profuse watery diarrhoea with no blood in faeces or dysentery with abdominal cramps, tenesmus and usually blood in stool; primary attack rate 7-76%, secondary cases rare; incubation period 1-11 d; unpasteurised milk most common vehicle or source in outbreaks, pork in sporadic cases; O3, O9, O8 and O5,27 predominant serotypes; 36-86% diarrhoea, 62-100% abdominal pain, 50-100% fever, 44-56% vomiting, 24-67% nausea, 18-60% headache, 22-31% pharyngitis, 11-38% rash, 15-38% joint pain, laparotomy in up to 17% of cases), 14% extraintestinal (throat, blood, urinary tract, central nervous system, wounds); causes bacteraemia and septicemia in iron overload, endocarditis, traveller's diarrhoea, enteritis, enterocolitis, gastroenteritis, terminal ileitis, erysipelas-like condition, erythema nodosum, maculopapular rash, mesenteric lymphadenitis, mycotic aneurism, myocarditis and pericarditis, reactive arthritis, infections in abnormal host; virulent strains bind congo red, bear plasmids of 40-50 MD, autoagglutinate, show reduced growth on magnesium oxalate agar, serum resistance, lethality for iron-stressed mice; transmitted in blood; treatment: cotrimoxazole, pefloxacin (MIC 0.25 mg/L), tobramycin, tetracycline; also susceptible to ciprofloxacin (0.03 mg/L), ofloxacin (< 0.06-0.12 mg/L), meropenem (0.06 mg/L), norfloxacin (0.1-0.5 mg/L), enoxacin (0.25-0.5 mg/L), imipenem (100%), cefamandole, cefoperazone, cefotaxime, ceftizoxime, mezlocillin, piperacillin, gentamicin, tobramycin, amikacin, chloramphenicol, amoxycillin-clavulanate, trimethoprim, nalidixic acid; usually resistant to ampicillin

Y.frederickseniі: VP, rhamnose and sucrose positive; isolated from water and human wounds; susceptible to fleroxacin (MIC 0.125-0.25 mg/L)

Y.intermedia: citrate, VP, rhamnose, sucrose, melibiose, α-methyl D-glucoside and raffinose positive; isolated from water and human wounds

Y.kristenseniі: VP negative; susceptible to fleroxacin (MIC $\leq$ 0.06 mg/L)

Y.pestis: salicin, β-glucosidase, β-D-galactosidase and maltose positive; VP, lysine decarboxylase, arginine dihydrolase, ornithine decarboxylase, phenylalanine, gas from glucose, lactose, inositol, rhamnose, Simmon's citrate, γ-glutamyl transferase, cellobiose, sorbitol, oxidase and H_2S negative; urease and sorbitol variable; causes plague, bacteraemia and septicemia, postneonatal pyogenic meningitis (rare complication of plague), pneumonitis, local and generalised sepsis, lymph gland infections (pea-sized to orange-sized inguinal, axillary), haemorrhagic fever; transmitted by bite from infected rodent flea; primarily pathogen of rodents; transfer to man caused greatest epidemic in human history (75 M deaths); envelope or capsular antigen (fraction I, carbohydrate-protein complex) and VW antigen complex inhibit phagocytic attachment and

ingestion; fraction I evokes protective antibodies under some conditions; antibodies to VW antigen are protective against strains that lack envelope antigen; extracellular protein toxin damages phagocytes; diagnosis: Gram stain, fluorescent antibody stain and culture of lymph node and bubo aspirate, blood cultures, sputum, CSF, urine, serum passive haemagglutination titres, ELISA; treatment: streptomycin, tetracycline

Y.pseudotuberculosis: motile at 20°C, nonmotile at 35°C; growth on MacConkey agar and Tergitol 7; salicin, arabinose (may be delayed), β-xylosidase, urease, rhamnose, β-D-galactosidase, H_2S, maltose and melibiose positive; VP, lysine decarboxylase, arginine dihydrolase, ornithine decarboxylase, phenylalanine deaminase, gas from glucose, lactose, inositol, sorbitol, oxidase, indole, sucrose, cellibiose and sorbose negative; Simmon's citrate variable; causes pseudotuberculosis, adult hepatitis, hepatic abscess, maculopapular rash, mesenteric lymphadenitis, reactive arthritis, infections in abnormal host; diagnosis: culture of appropriate specimen; treatment: cotrimoxazole, tetracycline, streptomycin; also susceptible to fleroxacin (MIC ≤ 0.06-0.125 mg/L), imipenem (100%), chloramphenicol, kanamycin

Y.ruckeri: lysine decarboxylase, melibiose, gelatinase, citrate, H_2S and maltose positive; urease, cellobiose, indole, sorbose and sorbitol negative

Order Legionellales

Family Coxiellaceae

Coxiella burnetii: causes Q fever (endocarditis, chronic hepatitis, low platelets, acute respiratory illness, pneumonia, encephalitis, meningoencephalitis, myocarditis and pericarditis, haemorrhagic fever, abortion, premature delivery, stillbirth); worldwide; vector ticks but does not require arthropod vector for transmission; reservoir bandicoot, sheep, cattle, goats, ? birds; human infections from direct or indirect contact with infected sheep, cattle, goats; Q fever^{+++}; typhus, RMSF, OX19, OX2 and OXK negative; enters across epithelial surfaces of respiratory tract, conjunctiva and ? intestinal tract; diagnosis: indirect fluorescent antibody titre, complement fixation test, ELISA; treatment: doxycycline, tetracycline, erythromycin, rifampicin, clindamycin, cotrimoxazole, lincomycin; also susceptible to trimethoprim

Family Legionellaceae

Fluoribacter: causes non-pneumonic legionnaire's disease; diagnosis: serology; treatment: erythromycin

F.dumoffii: includes TEX-L; recognised from clinical specimens; susceptible to rifampicin (MIC 0.03 mg/L), imipenem (0.12 mg/L), erythromycin (0.25 mg/L), cefotaxime (0.5 mg/L)

F.gormanii: recognised from clinical specimens

Legionella bozemanii: includes WIGA; recognised from clinical specimens

Legionella: rods of variable length; asporogenous; motile by 1 or more polar or lateral flagella; obligately aerobic; carbohydrates neither fermented nor oxidised; fastidious; no growth on standard blood agar or other commonly employed laboratory media; requires L-cystine and iron salts; charcoal yeast extract agar and buffered charcoal yeast agar used for isolation; slow growing (2-3 d); grows best in humidified air; some species require 2-5% CO_2 for optimal growth; at least 9 species recognised from clinical specimens; some reactions useful in distinguishing between species include indophenol oxidase activity, gelatinase production, blue-white fluorescence of growth on charcoal yeast extract agar under a Wood's lamp, β-lactamase detection by rapid chromogenic cephalosporin technique, browning of appropriate agar medium containing tyrosine, analysis of isoprenoid quinones; indirect fluorescent antibody test standard serological test to diagnose legionellosis; few laboratories expected to undertake separation of species; isolated from surface water, mud, moist soil adjacent to a body of water, from thermally polluted lakes and streams, from water collected from air conditioning cooling towers and evaporative condensers, and from hospital showers and nebulisers; not isolated from dry soil or animals; isolated from human lung, trachea, pleural fluid, sputum, blood and bronchial washing; causes pneumonia in humans (legionellosis, legionnaire's disease, Pittsburgh pneumonia; especially in T helper lymphocyte deficiency), nonpneumonic Pontiac fever, rhabdomyolysis, bacteraemia and septicemia (uncommon in neutropenics), endocarditis, systemic infections in cell-mediated immunity disorders; growth stimulated by excess iron; treatment: erythromycin or ciprofloxacin (MIC 0.125 mg/L) + rifampicin (0.015-0.5 mg/L); also susceptible to gatifloxacin, moxifloxacin, difloxacin (≤ 0.06-1 mg/L), ofloxacin (0.06 mg/L), azithromycin, clarithromycin, roxithromycin, doxycycline, tetracycline, minocycline, rifabutin

L.jordanis: recognised from clinical specimens

L.longbeachae: causes legionnaires' disease; associated with potting soil

L.oakridgensis: recognised from clinical specimens

L.pneumophila: respiratory pathogen in man; causes legionnaire's disease, pneumonia, acute sinusitis in AIDS, cellulitis (single case associated with pneumonia), infections in abnormal host (T cell deficiency); serogroups 1-6, group 1 most important; transmitted in water (aerosols, cooling towers, evaporative condensers), often acquired from contaminated air conditioning units; toxin inhibits phagocyte oxidative response; multiplies in macrophages; toxin damages cells, ? contributing to extrapulmonary disturbances in legionnaire's disease; interferon γ, tumour necrosis factor induce antimicrobial activity; diagnosis: microagglutination (significant titre ≥ 1:880), direct fluorescent antibody (lung tissue, pleural fluid), indirect fluorescent antibody (significant titre ≥ 1:256), ELISA (significant titre ≥ 1:40), radioimmunoassay, Dieterle silver stain, culture on charcoal yeast extract agar, guinea pig inoculation; treatment: erythromycin (MIC ≤ 0.6-1 mg/L), doxycycline,

rifampicin (0.008-0.06 mg/L), imipenem (0.015-0.06 mg/L), cefotaxime (≤ 0.12-0.25 mg/L), amoxycillin (0.12-1 mg/L), ampicillin (0.5-0.8 mg/L)

L.wadsworthii: recognised from clinical specimens

Tatlockia: causes non-pneumonic legionnaire's disease; diagnosis: serology; treatment; erythromycin

Legionella micdadei: does not produce β-lactamase; includes TATLOCK and HEBA; Pittsburgh pneumonia agent; nosocomial pneumonia, particularly in renal transplant and bone marrow transplant recipients; stains weakly acid fast in clinical specimens and when grown in liquid culture media; susceptible to rifampicin (MIC ≤ 0.008 mg/L), imipenem (≤ 0.015-0.06 mg/L), erythromycin (≤ 0.06-0.5 mg/L), cefotaxime (≤ 0.12-0.25 mg/L), amoxycillin (0.12-1 mg/L)

Order Pasteurellales

Family Pasteurellaceae

Actinobacillus: Gram negative coccobacillary to rod-shaped; asporogenous; nonmotile; facultatively anaerobic; fastidious; grows only on complex media; growth requires, or enhanced by, increased moisture, serum and/or CO_2; colonies sticky on primary isolation and occasionally difficult to remove from agar surface; ferments glucose, fructose and mannitol; positive for ONPG; nitrate reduction (no gas); indole not produced; parasites of mammals (including humans) and birds; causes bacteraemia and septicemia (uncommon in neutropenics)

A.capsulatus: capsules present; growth enhanced by CO_2; ferments glucose (no gas), xylose, lactose, maltose, sucrose and mannitol; positive test reactions for indophenol oxidase, catalase, urease and esculin; etiological agent of arthritis in rabbits

A.equuli: colonies extremely sticky; usually grows on MaConkey; ferments glucose (no gas), xylose, lactose, sucrose, maltose, mannitol, trehalose and melibiose; ONPG and urease only positive reactions in API; positive test reactions for indophenol oxidase and urease; catalase usually produced; esculin not hydrolysed; distinguished from *A.ligniersii* on basis of fermentation of trehalose and melibiose; natural habitat rumens of cattle and sheep; mostly of veterinary significance (arthritis, septicemia, nephritis in foals and pigs); isolated from animal-bite wounds and joint fluid of humans

A.lignieresii: usually grows on MacConkey; ferments glucose (no gas), xylose, lactose (slow), sucrose, maltose and mannitol, but not trehalose or melibiose; positive test reactions for indophenol oxidase and urease; usually produces catalase; esculin not hydrolysed; distinguished from *A.equuli* on basis of failure to ferment trehalose and melibiose; natural habitat rumens of cattle and sheep and oral mucosa of normal horses; mostly of veterinary significance; isolated from animal-bite wounds of humans

A.pleuropneumoniae: most strains require V factor (biovar 1), some do not (biovar 2); β-haemolytic on sheep blood agar; no growth on unsupplemented MacConkey; lactose not fermented; CAMP reaction positive; closely related to, and additional phenotypic properties the same as for, *A.lignieresii*; isolated from pigs, lambs and cattle; of veterinary significance

A.ureae: no growth on MacConkey; ferments glucose (no gas), sucrose, maltose and mannitol, but not xylose; indophenol oxidase and urease produced; variable test reactions for catalase; esculin not hydrolysed; normal habitat human respiratory tract; isolated from human sputum, bronchi, throat, trachea, nasal swab, sinus, blood, exudate, CSF, eye and in otitis media; associated infrequently with bronchiectasis and chronic bronchitis; occasionally associated with pneumonia, meningitis, septicemia, peritonitis, sinusitis and ozaena

Aggregatibacter

Actinobacillus actinomycetemcomitans: growth requires, or enhanced by, increased moisture and CO_2; growth in broth granular, with colonies adhering to sides of tubes; star-like colonies observed in older agar plate cultures; no growth on MacConkey; ferments glucose (with serum added), sometimes with gas; biotypes based on acid from xylose, maltose and mannitol; catalase produced; variable indophenol oxidase reaction; urease negative; natural habitat mucous membranes of humans; isolated from human blood, mandibular and submandibular abscesses and rib, neck and facial sinus; causes bacteremia and septicemia (associated with oral infection), cat and dog bite infections, cerebral abscess (uncommon), empyema, endarteritis, endocarditis (associated with periodontitis and prosthetic valves), endophthalmitis (in association with endocarditis), acute cystitis (in association with endocarditis), meningitis, vertebral osteomyelitis (uncommon), parotitis and submandibular sialadenitis (uncommon), myocarditis and pericarditis (rare), periodontal infection (dominant organism in juvenile periodontitis), pneumonia, skin and soft tissue infections (localised granulomatous lesions and abscesses; may be associated with infection due to *Actinomyces*), synovitis, thyroiditis; treatment: chloramphenicol (usually susceptible), tetracycline (usually susceptible), ampicillin, gentamicin (usually susceptible); also usually susceptible to carbenicillin, mezlocillin, cefazolin, cefotaxime, ceftriaxone, tobramycin, rifampicin

A.ureae: rarely pathogenic for humans

Aggregatibacter segnis: rods pleomorphic with filamentous forms; requires V factor only; growth not enhanced by CO_2; porphyrin test positive; ferments glucose (weakly), but not xylose or lactose; catalase reaction variable; urease, indole, indophenol oxidase and ornithine decarboxylase tests negative; natural habitat human oral flora, particularly in dental plaque; isolated from pancreatic abscess; a cause of appendicitis and endocarditis

Haemophilus aphrophilus: small rods or filaments; granular growth in broth, with colonies adhering to side of tube; colonies roughened surface with a centrally situated stellate imprint; X factor required both aerobically and anaerobically for primary isolation (some strains) or V factor required or neither X nor V factor required; requires, or growth stimulated by,

CO_2; nonhemolytic; oxidase usually negative, some strains positive; H_2S negative; ferments glucose (with slight gas), raffinose, lactose, melibiose, melizitose and sorbose, but not xylose or galactose; negative tests for catalase, indole, urease and ornithine decarboxylase; porphyrin reaction positive; occurs in human oral cavity and pharynx; isolated from mucous membranes and dental plaque of humans; pathogenic for humans (endocarditis, sinusitis, soft tissue wounds, septicemia, brain abscess, pneumonia, osteomyelitis and osteochondritis, crystalline keratrophy, cholecystitis, perinatal generalised disease, cat and dog bite infections, arthritis, endophthalmitis (in association with endocarditis), epiglottitis, paronychia); treatment: ampicillin + gentamicin; also susceptible to ciprofloxacin (MIC $\leq$ 0.03 mg/L), norfloxacin (0.03 mg/L), ofloxacin (0.03 mg/L), cotrimoxazole (0.03-1 mg/L), enoxacin (0.06 mg/L)

Avibacterium

Pasteurella avium: some strains require V factor; ferments trehalose and D-xylose (strain variable); negative test reactions for ornithine decarboxylase, indole and urease; isolated from chicken and calves

P.bettyae: coccoid to bacillary rods; asporogenous; nonmotile; facultatively anaerobic; fastidious; growth enhanced by CO_2; growth on MacConkey variable; indophenol oxidase (variable) and catalase produced; ferments glucose (with small amounts of gas) and fructose; positive test reactions for indole and nitrate (no gas); urease not produced; natural habitat unknown; isolated from a variety of human specimens, primarily genitourinary tract of females; isolated from a purulent Bartholin abscess

P.gallinarum: no V factor requirement; ferments trehalose and maltose; negative test reactions for ornithine decarboxylase, indole and urease; isolated from chickens; commensal of poultry and occasionally sheep and cattle

P.volantium: V factor required; ferments trehalose, maltose, mannitol, D-xylose (strain variable) and sorbitol (strain variable); ornithine decarboxylated by some strains; indole and urease not produced; isolated from fowl and humans (no site indicated)

Gallibacterium anatis: no V factor requirement; ferments trehalose, D-xylose and mannitol; negative test reactions for ornithine decarboxylase, indole and urease; isolated from intestinal tract of ducks

Haemophilus: Gram negative minute to medium-sized coccobacilli or rods of variable morphology, sometimes forming threads or filaments and showing marked pleomorphism; nonmotile; nonsporeforming; aerobic or facultatively anaerobic; often bipolar staining; polysaccharide capsules in many strains; fastidious, requiring preformed growth factors present in blood (X factor—protoporphyrin IX or protopene) and/or V factor—nicotinamide adenine dinucleotide); grows best on complex media, such as chocolate agar, supplemented with these growth factors; colonies usually nonpigmented or slightly yellowish, flat, convex and usually smooth; optimum temperature 35-37°C; may be β-hemolytic; indophenol oxidase strain variable; ferments carbohydrates; nitrate reduced to nitrite; normal flora of mouth, nasopharynx, throat; obligate parasite on mucous membranes of humans and a variety of animal species; causes arthritis, bacteraemia, brain abscess, purulent conjunctivitis, endocarditis (1% of primary), epiglottitis, laryngotracheobronchitis, meningitis, osteomyelitis, otitis media, pharyngitis, pneumonitis, sinusitis, venereal infections; predisposing factors age, sickle cell disease, splenectomy, agammaglobulinemia, treated Hodgkin's disease, alcoholism; treatment: amoxycillin/ampicillin (resistance noted; > 95% due to β-lactamase), cotrimoxazole; most strains susceptible to most antimicrobials except erythromycin and clindamycin; ciprofloxacin (MIC 0.015 mg/L), cefotaxime (resistance not yet reported), lomefloxacin (0.06 mg/L), enoxacin (0.25 mg/L), amoxycillin/clavulanate (< 5% resistance in Australia), chloramphenicol (< 5% resistance in Australia), cefaclor (< 5% resistance in Australia)

H.aegyptius: long, slender rods, sometimes filamentous; nonencapsulated; may take 2-4 d to grow on chocolate agar; requires X and V factors but no growth on tryptic soy agar with X and V factors added; growth not enhanced by CO_2; non-haemolytic; porphyrin test negative; ferments glucose (slow), but not xylose or lactose; urease produced; catalase and indophenol oxidase formed; indole and ornithine decarboxylase not produced; natural habitat unknown (? soil); causes acute or subacute purulent conjunctivitis and other eye disease, Brazilian purpuric fever, endocarditis; treatment: rifampicin

H.ducreyi: small, slender, Gram negative bacilli in pairs, chains, filaments or 'fish shoals'; growth very poor on most laboratory media, satisfactory on chocolate agar enriched with Isovitalex, very sparse on blood agar; growth enhanced by moisture and CO_2; requires X, but not V, factor; porphyrin reaction negative; slight haemolysis; colonies usually difficult to remove from agar surface; indophenol oxidase, but not catalase, produced; negative test reactions for urease, indole and ornithine decarboxylase; usually no acid from carbohydrates; causes chancroid (soft chancre; genital sore, lymph node suppuration; sexually transmitted; commoner in tropics and subtropics); diagnosis: microscopy and culture; treatment: ceftriaxone (MIC < 0.0005-0.03 mg/L), ciprofloxacin (0.0005-0.08 mg/L), cotrimoxazole (93-95% cure rate), erythromycin, tetracycline, sulphisoxazole, amoxycillin-clavulanate; also susceptible to rosoxacin (0.001-0.1 mg/L), norfloxacin (< 0.003-0.5 mg/L), pefloxacin (< 0.003-1 mg/L), ofloxacin (0.015-0.06 mg/L), fleroxacin (0.015-0.125 mg/L), enoxacin (0.015-0.25 mg/L)

H.haemoglobinophilus: small pleomorphic rods, sometimes with filaments; requires X factor only; porphyrin reaction negative; growth not enhanced by CO_2; grows as well on blood agar as on chocolate agar; nonhemolytic; ferments glucose and xylose, but not lactose; indophenol oxidase and catalase produced; indole formed; urease and ornithine decarboxylase tests negative; normal flora of dog's preputial sac and vagina; cause of human otitis media and osteomyelitis

H.haemolyticus: small coccobacilli or short rods, sometimes with filaments; X and V factors required; growth not enhanced by CO_2; β-haemolysis on horse and rabbit blood agar; porphyrin reaction negative; ferments glucose (usually with gas) and xylose (occasionally), but not lactose; urease, catalase and indophenol oxidase usually produced; indole production variable; ornithine decarboxylase not produced; natural habitat the nasopharynx of some healthy humans; clinical significance unknown

H.influenzae: Gram negative, slender coccobacilli or small rods; pleomorphic, sometimes with filaments; some strains encapsulated; X and V factors required; no haemolysis on blood agar; no growth on blood-free media; growth not enhanced by CO_2; porphyrin production negative; ferments glucose and usually xylose, but not lactose; catalase and usually indophenol oxidase produced; 6 biovars based on urease, indole and ornithine decarboxylase reactions; human commensal (present in human nasopharynx; type b in 3-8% of unvaccinated), invades damaged lung; causes abortion, abortional and puerperal infection, acute obstructive laryngotracheal infection, amnionitis, septic arthritis (in infants, young children and debilitated adults; type b), bacteraemia and septicemia (0.7-4% overall; 1.6-8% of neonatal (50-86% mortality); 90% nontypeable in neonates, mainly type b in older patients), bronchiectasis, acute bronchitis (non-type b and nontypeable strains), bursitis, cellulitis (type b; buccal associated with otitis media; cervical cellulitis in adults), cerebrospinal fluid shunt infections, chorioamnionitis, purulent conjunctivitis, acute endocarditis, IUD-related endometritis, empyema (type b), acute epididymitis and epididymoorchitis (mainly homosexual men and children), acute epiglottitis (type b; children), endophathalmitis (postoperative and conjunctival filtering-bleb associated), human bite and clenched fist infections, infections in abnormal host (γ-globulin dysfunction, splenic dysfunction), liver abscess in adults, mastoiditis, nasal septal abscess, perinatal generalised disease, post-neonatal pyogenic meningitis (children; usually type b; ≈ 2000 cases/y in USA; 46% of bacterial meningitis; incidence 1/100 000 (59/100 000 at age 6-8 months); case-fatality rate 7%), nasopharyngitis, osteomyelitis and osteochondritis (type b), otitis media (non-type b and nontypeable), pancreatic abscess, parametritis, pelvic abscess and pelvic inflammatory disease (IUD-related and maternal), pericarditis in adults (type b), peritonitis, peritonsillar abscess, pharyngitis, preseptal and postseptal cellulitis (< 5 y; following upper respiratory infection; usually type b), primary and secondary pneumonia (all types), chronic pulmonary infection in cystic fibrosis, pneumonitis, pulmonary abscess, pyomyositis (rare), septicaemic adrenal haemorrhage syndrome, acute and chronic maxillary sinusitis (non-type b and nontypeable), thyroiditis, tissue abscesses (type b), acute tracheitis, dysuria-frequency (acute urethral) syndrome, urethritis, urinary tract infection (non-type b and nontypeable), uvulitis (children), vaginitis, systemic infections in agammaglobulinemia, chemotactic defect, C1, 2, 3, 4, factor B deficiency, hyposplenism/splenectomy; probably a secondary role in chronic infection of upper and lower respiratory tract, paranasal sinuses, middle ears and conjunctivae; invasive infections in older children and adults most common in male Caucasians with ethanol abuse, bacteraemic infections most commonly presenting as pneumonia and non-bacteremic as cutaneous abscess/cellulitis; risk factors for invasive disease household crowding, large household size, child care attendance, low socioeconomic status, low parental education, school-aged siblings, African American, Hispanic, Native American, sickle cell disease, antibody deficiency syndromes, malignanacies, chemotherapy, immunodeficiency, HIV infection, functional asplenia, stem cell transplant, male; 80% of nosocomial isolates from lower respiratory tract; extracellular; attaches to respiratory epithelium; polysaccharide capsule resists phagocytosis (unless antibody present; antibody confers specific immunity) and digestion; type-specific capsular polyribophosphate associated with invasiveness; role of endotoxic factors unknown; primary bodily defence mechanism humoral immune responses (phagocytes +, alternative complement +, bactericidal activity +, immune adherence (phagocytosis) +++); recovery from primary infection due to antibody; diagnosis: latex agglutination, counterimmunoelectrophoresis (antigen), Gram stain, culture, Quellung reaction, coagglutination; susceptible to amoxycillin/ampicillin (28% resistance (due to β-lactamase) in Australia), amoxycillin-clavulanate (2% resistance in Australia), piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, cefaclor (6% resistance in Australia), cefuroxime, trimethoprim (10% resistance in Australia), cotrimoxazole (5% resistance in Australia), doxycycline (5% resistance in Australia), cephamandole, cefotaxime/ceftriaxone (0.6% resistance in Australia), cefepime, cefpirome, rifampicin, rifabutin, ceftazidime (0.06-0.125 mg/L), cefotetan, cefoxitin, aztreonam, amikacin, chloramphenicol (3% resistance in Australia), amifloxacin (≤ 0.004 mg/L), ofloxacin (0.015-0.03 mg/L), pefloxacin (0.015-0.06 mg/L), fleroxacin (0.03-0.06 mg/L), rosoxacin (0.05 mg/L), ciprofloxacin (100% at < 0.06 mg/L), gatifloxacin, moxifloxacin, tetracycline (5% resistance in Australia), minocycline, oxolinic acid (≤ 0.06 mg/L), mupirocin (0.06 mg/L), foramidocillin (0.06-0.12 mg/L), enoxacin (0.06-0.5 mg/L), norfloxacin (100% at < 0.12 mg/L), cefixime (≤ 0.25 mg/L), colistin (0.25 mg/L), temocillin (0.25-0.5 mg/L), imipenem (0.5 mg/L), meropenem, gentamicin (0.5 mg/L), ceftizoxime (< 1 mg/L), cefperazone (< 1 mg/L), moxalactam (< 1 mg/L), tobramycin (1 mg/L); variably susceptible to azithromycin, clarithromycin, roxithromycin

H.paracuniculus: arginine dihydrolase positive

H.parahaemolyticus: small rods, pleomorphic, usually filamentous; growth not enhanced by CO_2; distinct β-haemolysis on horse or sheep blood agar; V factor required; synthesises porphyrins; ferments glucose (sometimes with gas) but not xylose or lactose; urease and indophenol oxidase produced; ornithine decarboxylase and catalase reactions variable; indole not produced; similar to *H.parainfluenzae*; natural habitat human oral cavity and pharynx; associated with acute pharyngitis, purulent oral infection, endocarditis, gallbladder empyema and periorbital cellulitis

H.parainfluenzae: small pleomorphic rods, usually with long filaments; granular growth in broth by some strains; non-haemolytic; growth not enhanced by CO_2; V factor required; porphyrin test positive; ferments glucose (often with gas), but not lactose, xylose, ribose or trehalose; indophenol oxidase produced; catalase reaction variable; indole not formed; 3 biovars based on urease and ornithine decarboxylase reactions; natural habitat human oral cavity and pharynx; causes localised abscesses (brain (rare), skin, joints, liver), purulent arthritis, endocarditis, acute epiglottitis, meningitis, vertebral osteomyelitis, pneumonia, prostatitis, rhabdomyolysis, urethritis, infections in abnormal host; treatment: amoxycillin, amoxycillin-clavulanate, erythromycin, ampicillin, gentamicin; also susceptible to cotrimoxazole (MIC 0.03-1 mg/L), ofloxacin (0.25 mg/L), ciprofloxacin (100%), norfloxacin (100%), enoxacin (100%), gentamicin (100%), kanamycin (100%), colistin (100%), carbenicillin (100%), cephalothin (100%)

H.paraphrohaemolyticus: short to medium length rods with occasional filaments; requires V factor and increased CO_2; catalase produced; ornithine decarboxylase not produced; no gas from glucose; otherwise, identical to *H.parahaemolyticus*; isolated from human sore throat, ulcer of mouth, sputum and urethral discharge of adult males; associated with liver abscess

Mannheimia

Pasteurella haemolytica: taxonomic position uncertain; closely related to genus *Actinobacillus*; rods and coccoid forms; nonmotile; asporogenous; facultatively anaerobic; fastidious; usually β-haemolytic on primary isolation; usually grows on MacConkey agar; indophenol oxidase and catalase (variable) produced; ferments glucose, mannitol, maltose and other carbohydrates according to biovar; nitrate reduced; H_2S positive; negative test reactions for urease, arginine dihydrolase, lysine decarboxylase and indole; rarely pathogenic for humans; causes fowl cholera, pneumonia in cattle, sheep, goats, lambs and birds, septicemia in lambs

Pasteurella: small Gram negative rods and ovals occurring singly, in pairs or short chains, bipolar staining; nonmotile; nonsporeforming; usually no growth on MacConkey, no growth on SS; aerobic to microaerophilic or facultatively anaerobic; fastidious; occasional V factor-requiring species or strain; optimum temperature 35-37°C; colonies round, greyish or yellowish; colonies of some species rough; no haemolysis on sheep blood agar; oxidase and indole positive; ornithine decarboxylase usually negative; catalase usually produced; ferments glucose, fructose, galactose, mannose and sucrose but not sorbitol, rhamnose, m-inositol, salicin or adonitol; nitrate reduced (no gas); no hydrolysis of starch or esculin; arginine dihydrolase, lysine decarboxylase and gelatinase (except *P.dagmatis*) negative; urease negative (except *P.dagmatis*); parasite in vertebrates, particularly mammals (rarely humans) and birds; causes pasteurellosis (cat and dog bite infections, erythema nodosum, local and generalised sepsis); growth stimulated by excess iron; treatment: penicillin (resistance not yet confirmed in Australia)

P.caballi: Gram negative, oxidase positive, non-motile, fermentative, aerogenic, catalase negative coccobacillus; causes equine endocarditis; treatment: oxytetracycline, ampicillin, ceftiofur

P.canis: no V factor requirement; variable acid from trehalose and D-xylose; ornithine decarboxylase, but not urease, produced; indole production variable (biotype 1 indole positive, biotype 2 indole negative); found in oral cavities of dogs and calves and in dog-bite wounds of humans

P.dagmatis: no V factor requirement; ferments trehalose and maltose; positive test reactions for urease and indole; ornithine not decarboxylated; gelatine slowly liquefied (after 14 d); isolated from dogs and cats, as well as from human local and systemic infections resulting from animal bites; also causes endocarditis

P.multocida: no V factor requirement; no growth on MacConkey agar or Tergitol 7; indole, ornithine decarboxylase, mannitol, sucrose and H_2S positive; urease, β-D-galactosidase and maltose negative; fermentation of sorbitol and dulcitol differentiate 3 subspecies: subspecies *multocida* ferments sorbitol, not dulcitol; subspecies *septica* ferments neither carbohydrate; subspecies *galliarta* ferments both sorbitol and dulcitol; isolated from most mammals, including humans, and birds; causes infections in cat and dog bites, endophthalmitis (cat scratch), infant meningitis (rare; animal contact; case-fatality rate 30%), infant appendicial peritonitis, sinusitis, head surgery infection, psoas muscle abscess, polyarticular septic arthritis, infant and adult brain abscesses, osteomyelitis, infections in abnormal host, chronic pulmonary infections and septicemia in humans, acute septicemia and chronic infections in cats and dogs, haemorrhagic septicemia in cattle; inhibits phagocytic attachment and ingestion; susceptible to penicillins (95%) except flucloxacillin/dicloxacillin, amoxycillin-clavulanate (100%), cephalosporins, aminoglycosides, carbapenems, fluoroquinolones (95%), tetracyclines (95% susceptible), trimethoprim, cotrimoxazole (90% susceptible), aztreonam, chloramphenicol, rifampicin, rifabutin

P.pneumotropica: taxonomic position uncertain; closely related to genus *Actinobacillus*; nonmotile rods; asporogenous; facultatively anaerobic; fastidious; growth on MacConkey variable; indophenol oxidase and catalase produced; ferments glucose (no gas), xylose, sucrose, maltose, lactose (occasionally) and mannitol (rarely); positive test reactions for urease, indole (usually), nitrate (no gas) and ornithine decarboxylase; isolated from mice, rats and other small animals; rarely pathogenic for humans; isolated from human cellulitis, rabbit bite, throat, pleural fluid and lymph node; causes abscess, conjunctivitis, peritonitis, pneumonia, septicemia in laboratory rats, mice and guinea pigs and in cats and dogs, human septic arthritis and osteomyelitis and other infections resulting from dog and cat bites or exposure

P.stomatis: no V factor requirement; ferments trehalose; indole produced; urease and ornithine decarboxylase not produced; normal habitat throat, gum and tonsil of mammals; isolated from respiratory tracts of cats and dogs

***Pasteurella* species A:** V factor required; ferments trehalose and L-arabinose with variable acid production from maltose, D-xylose and mannitol; negative test reactions for ornithine decarboxylase, indole and urease; isolated from chickens and pigeons

***Pasteurella* species B:** V factor not required; ferments trehalose, maltose, D-xylose and dulcitol; ornithine decarboxylase and indole, but not urease, produced; isolated from cat and dog-bite wounds of humans

Unclassified Pasteurellaceae

Pasteurella aerogenes: taxonomic position uncertain; not related to genus *Pasteurella*; coccobacilli, filamentous; nonmotile; obligately anaerobic; fastidious; growth on MacConkey; indophenol oxidase and catalase produced; ferments glucose (with gas), xylose, sucrose and maltose; positive test reactions for urease, nitrate (no gas) and ornithine decarboxylase (usually); indole not produced; natural habitat intestine of pigs; associated with pig bite and leg ulcers of humans

Order Pseudomonadales

Family Moraxellaceae

Acinetobacter: rods very short and plump, approaching coccus shape in stationary phase, predominantly in pairs; asporogenous; nonmotile; catalase produced; oxidase negative; grows on MacConkey agar and brain heart infusions; obligately aerobic; some strains oxidise glucose and other carbohydrates; nitrate usually not reduced; lysine decarboxylase, arginine dihydrolase, ornithine decarboxylase and oxidase negative; most strains good growth on MacConkey; some strains β-hemolytic, proteolytic and grow on SS agar; free-living and widely distributed in nature; occurs naturally in soil, water and sewage; isolated from almost every conceivable source on or within the human body, usually as contaminants; normal flora of nasopharynx, colon, large intestine, ileum, female genitals (anterior urethra, vagina; adherence to labium majus +), skin; opportunistic pathogen implicated in a number of community-acquired, but primarily nosocial, infections, causing bacteremia and septicemia, burn infections, complications of instrumentation and surgery, purulent conjunctivitis, disease of newborn, acute epyema, endocarditis (rare), nosocomial postneonatal purulent meningitis, community-acquired pneumonia, urethritis, endotoxic reactions associated with reuse of cardiac catheters, miscellaneous local septic reactions, abscess, cellulitis, synovitis, osteomyelitis, ventriculitis, teacheitis, infections in abnormal host (various complications in immunocompromised individuals), nosocomial infections; predisposing factors tracheostomy, ventilator therapy, broad-spectrum antimicrobial therapy, multiple indwelling catheters, old age, underlying chronic disease; growth stimulated by excess iron; treatment: imipenem (MIC 0.25-0.5 mg/L), ciprofloxacin, gentamicin, tobramycin; also susceptible to piperacillin, piperacillin-tazobactam, ticarcillin-clavulanate, amikacin, meropenem, gatifloxacin, moxifloxacin, cotrimoxazole (0.25 mg/L), amifloxacin (1 mg/L); variably susceptible to cefotaxime, ceftriaxone, cefipime; 98% intrinsic resistance (due to β-lactamase) to amoxycillin, ampicillin, amoxycillin-clavulanate, cephalothin, cephalexin (possibly all resistant in clinical practice)

A.baumannii: causes 21% of ventilator-associated pneumonia, nosocomial bacteremia and septicaemia; resistant strains reported susceptible only to polymyxin and sulbactam

A.calcoaceticus: causes acute tracheitis, acute empyema, local and generalised sepsis, cellulitis, endocarditis, osteomyelitis, purulent conjunctivitis

A.johnsonii: causes vascular catheter-related bacteremia and septicemia

Subgenus *Branhamella*

Moraxella catarrhalis: Gram negative coccus, single or in pairs with adjacent sides flattened; tendency to resist Gram decolourisation; non-motile; asporogenous; usually aerobic but some strains facultatively anaerobic; growth on media devoid of blood, no growth on Thayer-Martin medium; colonies nonpigmented or grey; growth at 22°C; catalase, indophenol oxidase and DNAse produced; most strains reduce both nitrate (distinguishes from *Neisseria*) and nitrite (no gas); agglutination in saline; natural habitat nasal cavity of humans; isolated from human eye, sputum, blood, ear, throat and nose; causes bacteraemia and septicemia in immunodeficient (rare), bronchopulmonary infection, bronchitis, respiratory infections in compromised host, acute otitis media in infants and children, acute maxillary sinusitis, tracheitis, pneumonia, postneonatal purulent meningitis, endocarditis, conjunctivitis, endophthalmitis (postoperative), urethritis, septic arthritis (rare) and, occasionally, systemic infections; growth stimulated by excess iron; susceptible to amoxycillin-clavulanate (resistance not yet confirmed in Australia), piperacillin-tazobactam, ticarcillin-clavulanate, erythromycin (3% resistance in Australia), cefaclor, cefuroxime, cefepime, cefpirome, doxycycline, tetracycline (0.8% resistance in Australia), minocycline, aztreonam, chloramphenicol, cotrimoxazole (7% resistance in Australia), cefotaxime (resistance not yet confirmed in Australia), ceftriaxone (resistance not yet confirmed in Australia), cefotetan, ciprofloxacin (100% at 0.03 mg/L), gatifloxacin, moxifloacin, enoxacin (100%), norfloxacin (100%), ceftazidime (resistance not yet confirmed in Australia), pefloxacin (MIC 0.015-0.25 mg/L), cefoxitin (< 0.06-0.25 mg/L), difloxacin (0.12 mg/L), fleroxacin (0.125-0.5 mg/L), cefuroxime (0.125-1 mg/L), ofloxacin (0.13 mg/L), cefixime (≤ 0.25 mg/L), chloramphenicol (0.25-0.5 mg/L), rifampicin, amikacin, gentamicin, tobramycin, kanamycin, mezlocillin, imipenem, meropenem, azithromycin, clarithromycin, erythromycin, roxithromycin; 94% acquired resistance (via β-lactamase) to penicillin, ampicillin and amoxycillin (possibly all resistant in clinical practice); 98% intrinsic resistance to trimethoprim (possibly all resistant in clinical practice)

M.caviae: associated with animals; no carbohydrates fermented; growth at 22°C

M.cuniculi: associated with animals

M.ovis: associated with animals

Subgenus *Moraxella:* rods very short and plump approaching coccus shape, usually in pairs and short chains; tendency to resist Gram decolourisation; nonmotile; asporogenous; obligately aerobic; growth on MacConkey scant or negative; most strains fastidious in growth requirements, some require serum supplementation; colonies not yellow; oxidase positive; citrate negative; some isolates produce urease, phenylalanine deaminase and liquify serum, but majority lack extracellular hydrolytic enzymes; catalase produced except for some strains of *M.atlantae* and *M.bovis*; a few strains reduce nitrate to nitrite; normal flora of nasopharynx, nose, vagina, eye; causes transient bacteraemia, conjunctivitis, eye disease, rarely postpartum, postoperative and neonatal complications; growth stimulated by excess iron; usually susceptible to penicillin and most other antimicrobials, including gentamicin (MIC $\leq$ 0.03-0.25 mg/L), tetracycline (0.25 mg/L), neomycin (0.5 mg/L), ciprofloxacin (0.5 mg/L), norfloxacin (1 mg/L), imipenem (96% sensitive)

M.atlantae: serum required (variable) for growth on agar media; usually grows on MacConkey agar (may be delayed), but not in O-F basal medium; colonies small, semi-opaque, slightly pink, occasionally corroding and spreading; 1/3 of strains catalase positive; phenylalanine, urease, nitrate and gelatine negative; natural habitat unknown; isolated primarily from human blood and CSF, also lung tissue, sputum, urine, ear, nose and throat, wound, eye; clinical significance unknown

M.bovis: produces β-haemolysis on human blood agar and rabbit blood agar; growth on MacConkey agar; colonies either small, flat, corroding or larger, convex, butyrous, noncorroding and nonspreading; liquefies coagulated serum (Loeffler slant); nitrate reduction variable; 1/3 of strains catalase positive; phenylalanine positive; urease negative; hydrolyses gelatine; isolated from bovine eyes, both from unaffected eyes and cases of keratoconjunctivitis

M.lacunata: Gram negative, coccobacillary, does not require X or V factors, may not grow on media not containing blood or serum (counteracts toxic effect of certain components of peptone); no growth in O-F basal medium or on MacConkey agar; colonies small to large, translucent to semi-opaque, and occasionally ? pitting; catalase and oxidase positive; urease negative; phenylalanine deaminase variable; reduces nitrate (no gas); gelatine hydrolysis variable; liquefies coagulated serum (Loeffler slope); natural habitat upper respiratory tract and eyes of humans; rarely isolated; isolated from eye, blood, sputum, ear, nose, throat, CSF; causes purulent conjunctivitis, keratitis and iritis, meningitis, otitis media, sinusitis, infections in abnormal host

M.nonliquefaciens: coagulated serum not liquefied, otherwise similar to *M.lacunata*; some strains require addition of serum to peptone media; reduces nitrate (no gas); no growth in O-F basal medium or on MacConkey agar; colonies small to large, translucent to semi-opaque, occasionally mucoid and occasionally corroding and spreading; natural habitat human nasal cavity; a well-established parasite of humans and rarely causes disease; associated with endophthalmitis and pneumonitis with pulmonary abscess; isolated from ear, nose, throat, eye, sputum, blood, urine, CSF, wound

M.osloensis: utilisation of acetate in a mineral base medium without growth factor supplement distinguishes this species from other *Moraxella*; most strains grow in O-F basal medium and on MacConkey agar; colonies semi-opaque; alkalises sodium acetate slant; catalase positive; urease and gelatinase negative; phenylalanine deaminase variable; some strains reduce nitrate (no gas); natural habitat human pharynx; isolated from such clinical specimens as blood, genital swab, throat, CSF, urine, wound swab, pyogenic lesion, sputum, chest cavity, eye, nasopharyngeal swab and rectal swab; usually a harmless parasite but causes osteomyelitis, endocarditis, septicemia, meningitis, stomatitis and septic arthritis

Psychrobacter immobilis: non-motile, Gram negative coccobacilli or short to long rods, diplo forms; asporogenous; obligately aerobic; growth on Macconkey (may be sparse); chiefly psychrotrophic and unable to grow at 35°C or 37°C; nonmotile; many strains oxidise glucose, xylose, lactose and several other carbohydrates, but not sucrose, maltose or mannitol; positive test reactions for catalase, indophenol oxidase, urease, nitrate (variable; nitrogen gas not produced) and phenylalanine deaminase; indole and gelatinase not produced; Simmon's citrate and esculin negative; TSI alkaline/ no change; growth in 0% NaCl and 6% NaCl; an odour resembling that of a phenylethytl alcohol blood agar plate usually present; may have odour of rose; a few strains with an optimal growth temperature of 35°C similar to *Paracoccus yeei* strains; transformation studies required to identify such strains definitively; isolated from sea water, fish, fish slime, sausage, ground beef, poultry and air-contaminated agar media; a few strains with an optimal growth temperature of 35°C isolated from pathological specimens derived from both animals and humans; human sources include blood, brain tissue, urethra, wound, CSF, vagina and eye; no conclusion as to clinical significance; susceptible to penicillin

Psychrobacter phenylpyruvicus: production of urease distinguishes this species from *Moraxella*; catalase and phenylalanine deaminase positive; gelatine hydrolysis negative; most strains reduce nitrate (no gas); growth occurs in O-F basal medium and usually on MacConkey agar; colonies relatively small, often semi-opaque and slightly pink; natural habitat probably animals; isolated from human urine, urogenital tract, blood, CSF, skin, superficial lesion, pyogenic lesion, peritoneal fluid, ear, joint, sputum; clinical significance uncertain

Family Pseudomonadaceae: Gram negative aerobic and facultatively anaerobic bacilli, motile, polar monotrichous or tuft of flagella, nonsporeforming, nonfermentative, oxidise carbohydrates to acid but not gas, catalase positive; water-borne; cause infections in patients with interrupted integument

Pseudomonas: straight or slightly curved rods; asporogenous; obligately aerobic; motile with polar monotrichous or polar tuft of 1-6 or more flagella; growth on MacConkey, growth on SS, nitrate may be reduced to nitrite, lysine decarboxylase

and ornithine decarboxylase negative, arginine dihydrolase positive, special growth factors not required, catalase produced, usually oxidase positive, nonfermentative metabolism (some species oxidative in carbohydrates, others non-oxidative), DNAse negative, PHB variable, indole not formed, pigments variable (some species produce various fluorescent and nonfluorescent pigments, but no photosynthetic pigments); widely distributed in nature; causes abortional and puerperal infections, cellulitis, cerebrospinal fluid shunt infections, cholangitis and cholecystitis (rare), acute cystitis, 3% of primary endocarditis, endotoxic reactions associated with reuse of cardiac catheters, chronic eye infections, endophthalmitis (postoperative), human bite and clenched fist infections, neonatal meningitis, peritonitis (primary, secondary, peritoneal dialysis), pneumonia, localised skin lesions in septicemia and endocarditis, local and generalised sepsis, symbiotic gangrene, transfusion reactions due to bacterial contamination of blood and blood products, water-related infections, systemic infections in microbicidal abnormality, 9% of nosocomial infection (interrupted integument); growth stimulated by excess iron; treatment; ticarcillin + gentamicin, ciprofloxacin; also susceptible to norfloxacin (MIC 1 mg/L), imipenem (< 5% resistance in Australia); 100% intrinsic resistance to penicillin, flucloxacillin, clindamycin, erythromycin

P.aeruginosa: produces water-soluble, yellow-green (pyoverdin), yellow-brown or colourless fluorescent pigments; grows at 42°C, not at 4°C; motile with a single polar flagellum; nitrate reduced to nitrite and nitrogen gas; glucose oxidised; maltose, sucrose, lactose, starch, lysine decarboxylase, ornithine decarboxylase and H_2S negative; gluconate oxidation, gelatinase, and indophenol oxidase positive; methionine not required, alkaline phosphatase heat resistant, arginine dihydrolase synthesised, citrate positive; identified on basis of the characteristic grapelike odour of aminoacetophenone, the structure of colonies on agar medium and production of pyocyanin (a water-soluble, blue, nonfluorescent phenazine pigment); water-soluble, nonfluorescent red (pyorubin) and brown (pyomelanin) pigments occasionally produced; number of colonial variants (smooth, coliform-type, rough, mucoid, gelatinous) arising by dissociation of a single strain gives the false impression of different bacterial species present; most strains grow on cetrimide; widely distributed in soil, water, sewage and plants; common human intestinal bacterium (large intestine, lower ileum); adherence to nasal mucosa +++, labium majus ++; cause of disease in humans, as well as in certain animals, insects and plants; associated with 5% of all community-acquired infections, but infection usually restricted to hospitalised patients with predisposing conditions (14% of nosocomial infections (25% of Gram negative bacilli); important cause of fatal bacteraemia in neutropenic patients; causes bacteraemia and septicemia (especially associated with haemodialysis), severe epidemic diarrhoea of infants, burn infections, cellulitis, cranial parameningeal deep fascial space infections (immunocompromised and otogenic), acute empyema, ecthyma gangrenosa, endocarditis (14% of cases in drug addicts, 4% in children), endotoxinemia, acute epididymitis and epididymoorchitis, eye infection (iridocyclitis, keratitis and iritis, corneal ulcer, purulent conjunctivitis, panophthalmitis), folliculitis (polymorphous rash associated with spas and whirlpools), gastroenteritis, local and generalised sepsis, neonatal and postneonatal purulent meningitis, mycotic aneurism, myocarditis and pericarditis, nasal septic abscess, 3% of necrotising fascitis, 3% of osteomyelitis and osteochronditis, 35-70% of otitis externa ('swimmer's ear' and malignant), otitis media (malignant, chronic and complicating endotracheal intubation and mechanical ventilation), dermatitis, paronychia, perianal and perirectal abscess in patients with malignant disease, primary and secondary pneumonia, chronic pulmonary infection in cystic fibrosis (especially mucoid strains), postoperative complications, septic arthritis (complicating foot puncture wounds in children; in i.v. drug abusers), septicaemic adrenal haemorrhage syndrome, acute sinusitis, pulmonary abscess, 8% of thrombophlebitis, typhlitis, thyroiditis, wound infections including 5% of surgical wound infections (summer peak), urinary tract infections (pyelonephritis, cystitis, urethritis), infections in abnormal host (granulocytopenia, opsonophagocytic antibodies, local immunity (eg., cystic fibrosis), depressed/defective cell-mediated immunity, interrupted integument, surgical procedure), systemic infections in granulocytopenia; endotoxin A and cell-bound lecuocidin kill macrophages; inhibits phagocytic chemotaxis; 'surface slime' (polysaccharide) resists phagocytosis (unless antibody present) and digestion (associated with invasiveness; virulence factor); collagenase (virulence factor) causes spread of infection; elastase (virulence factor) causes necrotising vasculitis; other virulence factors pili, exotoxin A, haemolysin, lecithinase and lipase; potential virulence factors exotoxins B and C, protease; primary bodily defence mechanism humoral immune responses (immune adherence (phagocytosis) +++, phagocytes +, alternative complement (natural antibody) +, ? interference with adherence +); diagnosis: culture, counterimmunoelectrophoresis (serum; sensitivity 100%); susceptible to ticarcillin (13% resistance in Australia), tobramycin (5% resistance in Australia), gentamicin (17% resistance in Australia), ciprofloxacin (13% resistance in Australia, 38% in USA), norfloxacin (8% resistance in Australia, 37% in USA), ceftazidime (10% resistance in Australia), azlocillin (commonly susceptible), amikacin (13% resistance in Australia), colistin, neomycin (topical), piperacillin (9% resistance in Australia), imipenem (17% resistance in Australia), meropenem, ofloxacin, piperacillin-tazobactam (9% resistance in hospitals in Australia), ticarcillin-clavulanate; variably susceptible to gatifloxacin, moxifloxacin; resists many antibiotics—uniform resistance to penicillin results from exclusion by cell membrane and chromosomally mediated penicillinase; 100% intrinsic resistance to ampicillin, amoxycillin, amoxycillin-clavulanate, cephalosporins except cefepime, ceftazidime and cefpirome, cotrimoxazole and trimethoprim; possesses a Class I chromosomal β-lactamase but low mutation rate to resistance (10^{-9}) and not likely to give rise to mutants except in a sequestered site (cystic fibrosis, osteomyelitis)

P.alcaligenes: motile with a single polar flagellum, wavelength of the flagellum $\approx$ 1.6μm; indophenol oxidase produced; nitrate reduction (no gas) strain variable; urease not produced; non-oxidative in carbohydrates; alkali accumulates in O-F

fructose, which distinguishes *P.alcalignes* from related *P.pseudoalcaligenes*, which oxidises fructose; isolated from water and a variety of clinical specimens, primarily urine, blood and sputum; occasionally, an opportunistic agent; cause of empyema, neonatal septicemia, intrauterine infection, chronic pulmonary infection in cystic fibrosis, endocarditis in bone marrow transplant recipients

P.fluorescens: oxidase positive; produces water-soluble, yellow-green, yellow-brown or colourless fluorescent pigments (pyoverdins); arginine dihydrolase produced; gelatinase positive, gluconate variable, does not grow at 42°C, grows at 4°C; motile by polar tuft of 3 or more flagella; nitrate reduced to nitrite (few strains occasionally to nitrogen gas); oxidative in glucose and sucrose and certain other carbohydrates, maltose variable, lactose and starch negative; methionine not required; alkaline phosphatase heat resistant; proteolytic; failure to produce pyocanins and to grow at 42°C and possession of polar tuft of flagella distinguishes from closely related *P.aeruginosa*; isolated from soil, water, hospital environment and human clinical specimens, primarily from respiratory tract; causes bursitis, cat and dog bite infections, transfusion reactions due to bacterial contamination of blood and blood products, infections in abnormal host; susceptible to gentamicin (MIC $\leq$ 0.03-1 mg/L), ciprofloxacin (0.5-1 mg/L), norfloxacin (85%), enoxacin (85%); resistant to amoxycillin, amoxycillin-clavulanate, cefaclor, cefixime, cefuroxime, cephalexin

P.luteola: rods motile with a polar tuft of 1-6 or more flagella; asporogenous; obligately aerobic; catalase, but not indophenol oxidase, produced; indole not formed; oxidative in glucose and a wide range of other carbohydrates; colonies rough and/or smooth, with a water-insoluble pigment; distinguished from phenotypically similar *P.oryzihabitans* by positive test reactions for nitrate reduction (no gas) and hydrolysis of ONPG, esculin and arginine (variable); usually not found in general environment; saprophytes or commensals of humans; isolated from a variety of human clinical specimens, including nose, blood, throat, gallbladder, urine, CSF and penis; associated with septicemia, subdiaphragmatic abscess and prosthetic valve endocarditis in patients with predisposing diseases and peritonitis in continuous ambulatory peritoneal dialysis; cause of septicemia in an otherwise healthy patient with granulomatous hepatitis, bacteremia and septicemia associated with prosthetic materials and corticosteroids

P.mendocina: colonies flat, smooth, butyrous and non-wrinkled; forms a brown-yellow intracellular carotenoid pigment; motile with a polar flagellum; indophenol oxidase produced; nitrate reduced to gas; oxidative in glucose and xylose, not maltose; arginine dihydrolase produced; starch not utilised; distinguished from similar strains of *P.stutzeri* by colonial morphology and reactions for maltose, starch and arginine; a polar monotrichous flagellum and growth at 42°C distinguishes from phenotypically similar denitrifying strains of *P.fluorescens*; isolated from soil, water and urine; association with infections in humans unknown

P.oryzihabitans: rods motile with a single polar flagellum; asporogenous; obligately aerobic; catalase, but not indophenol oxidase, produced; indole not formed; oxidative in glucose and a wide range of other carbohydrates; colonies smooth and/or rough with a yellow intracellular pigment; distinguished from phenotypically similar *P.luteola* by negative test reactions for nitrate reduction and hydrolysis of ONPG, esculin and arginine; found in general environment; saprophytes of humans and other warm-blooded animals; isolated from rice paddies and rice flour, from respiratory therapy equipment and sink drains in the hospital, and from various human specimens, including pus, conjunctiva, pleural fluid, maxillary sinus washing, pleural aspirate, blood, ear, finger exudate, eye and breast drainage; associated with septicemia in a postneurosurgical patient, peritonitis in patients undergoing continuous ambulatory peritoneal dialysis, septicemia in a patient with severe digestive haemorrhage and isolated from a patient with metastatic gastric carcinoma; causes abscesses, bacteraemia and septicemia (prosthetic materials, corticosteroids), wound infections; susceptible to gentamicin (MIC $\leq$ 0.03-0.13 mg/L)

P.pertucinogena: motile with a polar flagellum; grey colonies on Bordet-Gengou medium mimic colonies of rough phase IV strain of *Bordetella pertussis*; colonies on trypticase soy agar semitranslucent, entire and glistening; nonoxidative in carbohydrates; produces indophenol oxidase, phenylalanine deaminase and pertucin, a bacteriocin that inhibits growth of *Bordetella pertussis*; susceptible to most antimicrobials except novobiocin; source not recorded, probably human respiratory tract; clinical significance unknown

P.pseudoalcaligenes: motile with a single polar flagellum; indophenol oxidase produced; nitrate usually reduced (no gas); urease usually not produced; weak oxidation of fructose in O-F medium differentiates from closely related *P.alcaligenes*; most other carbohydrates not utilised; isolated from various water sources and human blood, urine, throat, sputum and abscess; occasionally an opportunistic agent; associated with meningitis, postoperative knee infection, pneumonitis, septicemia and intrauterine infection

P.putida: produces water-soluble, yellow-green, yellow-brown or colourless fluorescent pigments (pyoverdins); indophenol oxidase and arginine dihydrolase produced; nitrate not reduced; glucose positive, maltose variable, gelatine negative; nonproteolytic activity distinguishes from proteolytic *P.fluorescens*; failure to produce pyocyanin and to grow at 42°C and possession of a polar tuft of 3 or more flagella distinguishes from closely related *P.aeruginosa*; isolated from soil, water, hospital environment and human clinical specimens, primarily from respiratory tract; rarely opportunistic; associated with infections of extremities, bacteraemia, septic arthritis and septicemia following blood transfusion; newly recognised as pathogen in cancer patients; susceptible to gentamicin (MIC $\leq$ 0.03-1 mg/L), enoxacin (85%), norfloxacin (85%); resistant to amoxycillin, amoxycillin-clavulanate, cefaclor, cefixime, cefuroxime, cephalexin

P.stutzeri: most freshly isolated strains produce dry, wrinkled, tough and adherent colonies, smooth colonies and various intermediate colony types; colonies usually buff to yellow to light brown due to high concentration of cytochrome c in cells; fluorescent pigment absent; motile with a single polar flagellum; usually growth at 42°C, no growth at 4°C, nitrate reduced to nitrite and nitrogen gas; grows under anaerobic conditions in nitrate-containing media accompanied by nitrogen gas production; oxidation in glucose, maltose and certain other carbohydrates, but not lactose; starch usually hydrolysed; oxidase positive; salt tolerant and non-halophilic but requires sodium cation for growth; methionine not required for growth; alkaline phosphatase heat sensitive; arginine dihydrolase and gelatinase not produced; susceptible to polymyxin; isolated from soil, water, hospital environment such as deionised water and aqueous green soap, and numerous clinical specimens including wound, ear, blood and CSF; part of increased flora during myelosuppressive chemotherapy; occasionally associated with infections in humans, including postoperative and posttraumatic infection of extremities, otitis media, conjunctivitis, septic arthritis, pneumonia, osteomyelitis and septicemia; susceptible to sisomicin (MIC 0.06-0.5 mg/L), ciprofloxacin (0.5 mg/L), gentamicin (0.13-1 mg/L), pefloxacin (1 mg/L), cefotetan (1 mg/L), cefoperazone (1 mg/L), ceftriaxone (1 mg/L), enoxacin (85%), norfloxacin (85%), amoxycillin, amoxycillin-clavulanate; resistant to cefaclor, cefuroxime, cephalexin

Order Thiotrichales

Family Francisellaceae

Francisella novicida: rarely associated with human infection

F.tularensis: small Gram negative rods and ovals, bipolar staining (though takes stain poorly); asporogenous; nonmotile; nonencapsulated; obligate aerobe; fastidious; cysteine or cystine either required or stimulating for growth; usually not cultured on conventional laboratory media; glucose cystine agar with thiamine and blood, cystine heart agar with blood, cystine yeast extract agar with α-ketoglutarate, chocolate agar with Isovitalex and Thayer-Martin medium support growth; catabolism of carbohydrates slow with production of acid (no gas); catalase (usually), but not indophenol oxidase, produced; identification confirmed by slide agglutination and/or direct fluorescent antibody tests; widely distributed in nature; found in all continents throughout world except Australia and Antarctica; isolated from approximately 100 types of wildlife; isolated from human blood, lymph node, pleural fluid, eye, lung and bone marrow; causes tularemia, bacteraemia and septicemia, meningitis (rare), pneumonitis, localised skin lesions, acute skin ulcers, cat and dog bite infections, hepatic granuloma, lymph gland infections (painful neck, axillary, epitrochlear) in humans; usually transmitted from wild animals (rabbits, hares, squirrels, moles, muskrats, beavers, deer, woodchucks), sheep, cattle, cats, birds, amphibians, fish, ticks, deerflies, mosquitoes to humans following handling of infected animals, insect bites or ingestion of contaminated meat or water; very infectious in laboratory; endotoxins present; diagnosis: culture of nodules, pustules, ulcers, lymph node aspirate, blood, pleural exudate or sputum on glycine-cystine agar, fluorescent antibody staining of exudates, microagglutination; treatment: streptomycin, tetracycline

Order Vibrionales

Family Vibrionaceae: flagellated at poles only

Allomonas enterica: straight or slightly curved rods; motile with a single polar flagellum, occasionally nonmotile; asporogenous; facultatively anaerobic (metabolism both respiratory and fermentative); no growth in media without NaCl (tolerates 5% NaCl); brown, nondiffusing pigment after growth at room temperature; indophenol oxidase and catalase produced; acid from glucose (no gas) and sucrose, but not lactose; positive test reactions for indole, amylase, gelatinase and ornithine decarboxylase (usually); negative test reactions for lysine decarboxylase, phenylalanine deaminase and urease; isolated from faeces of healthy humans, river water and sewage

Grimontia

Vibrio hollisae: motile with a single polar flagellum or nonmotile; requires NaCl for growth (tolerates 6% NaCl); variable growth on MacConkey, no growth on TCBS agar; ferments glucose (no gas), not lactose or sucrose; indophenol oxidase produced; positive test reactions for indole and ONPG; negative test reactions for lysine decarboxylase and ornithine decarboxylase, arginine dihydrolase (usually) and urease; nitrate reduced to nitrite; citrate, VP, gelatine, mannitol, inositol, sorbitol, rhamnose, melibiose and amygdalin negative; causes gastroenteritis (diarrhoea) and bacteraemia (rare) following ingestion of seafood, rare wound infections

Listonella

Vibrio anguillarum: motile with a single polar flagellum; requires NaCl for growth (tolerance of 6% NaCl strain variable); grows on MacConkey (slow) and TCBS agars; ferments glucose (no gas), sucrose, maltose and mannitol, but not lactose; indophenol oxidase produced; positive test reactions for ONPG, indole, arginine dihydrolase and VP; lysine and ornithine not decarboxylated; O/129 susceptible; causes disease of marine fish and eels

V.pelagius: O/129 susceptible

Photobacterium: no sheath on flagellum; PHB positive; HB and amylase negative; no pigment; variable oxidase

P.damselae: motile with a single polar flagellum; requires NaCl for growth (tolerates 8% NaCl); grows on MacConkey; ferments glucose (no gas) and maltose, but not lactose; indophenol oxidase, arginine dihydrolase and urease produced; lysine decarboxylase strain variable; negative reactions for indole, ornithine decarboxylase and ONPG; nitrate reduced to nitrite; citrate, mannitol, inositol, sorbitol, rhamnose, melibiose, amygdalin and arabinose negative; causes wound infection, local and

generalised sepsis following exposure of wounds to brackish water or injury by saltwater animals; mortality rate 25%; treatment: tetracycline, chloramphenicol

Vibrio: Gram negative straight or curved rods, motile by monotrichous or multitrichous polar flagella; on solid media, lateral flagellum in some species; sheath on flagellum; facultatively anaerobic (capable of both respiratory and fermentative metabolism); colonies convex, smooth, creamy white with entire edges; growth on MacConkey, usually no growth on SS; most species grow on a wide range of commonly used laboratory media provided they contain 0.5-1% NaCl; lysine decarboxylase, ornithine decarboxylase, indole, PHB and HB positive; arginine dihydrolase negative; ferments glucose to acid (generally no gas); all species growth stimulated by, and most require, sodium ion; susceptible to O/129 vibriostatic compound; variable amylase and pigment; most species oxidase positive and reduce nitrate (no gas); found in aquatic habitats throughout the world, including marine and estuarine environments, fresh water habitats and on surface and in intestinal contents of marine animals; pathogenic for marine vertebrates and invertebrates as well as for humans; causes profuse watery diarrhoea (no blood in stool), cellulitis, septicemia, otitis externa, thrombophlebitis, water-related wound infections; treatment: tetracycline; also susceptible to ciprofloxacin (< 5% resistance in Australia)

V.alginolyticus: motile with a single polar flagellum; requires NaCl for growth, grows in 10% NaCl; swarming on solid complex media; grows on MacConkey and TCBS agars; ferments glucose (no gas), sucrose, maltose and mannitol, not lactose; indophenol oxidase produced; positive test reactions for indole and decarboxylases for lysine and ornithine; VP reaction usually positive; ONPG and arginine not hydrolysed; inositol, sorbitol, rhamnose and melibiose negative; partially susceptible to O/129; causes cellulitis, otitis externa, marine-associated wound infections (71% of infections), local and generalised sepsis, gastroenteritis (12% of infections), conjunctivitis, intracranial infections; treatment: ciprofloxacin, tetracycline, chloramphenicol; also susceptible to fleroxacin (MIC $\leq$ 0.06-0.125 mg/L)

V.campbellii: O/129 partially susceptible

V.cholerae: motile with a single polar flagellum; grows on MacConkey and TCBS; ferments maltose, mannitol; does not require NaCl (tolerates 3% NaCl); indophenol oxidase produced; positive test reactions for ONPG, lysine decarboxylase and ornithine decarboxylase; arginine dihydrolase not produced; gelatinase, glucose (no gas), indole, sucrose and mannitol positive; phenylalanine deaminase, salicin, inositol, sorbitol, rhamnose, melibiose, arabinose, lactose (occasionally positive) and urease negative; VP variable; causes epidemic Asiatic cholera (O1 strains; 8M cases with 122 000 deaths (31% in children < 5 y) globally annually), gastroenteritis (non-O1 strains), traveller's diarrhoea (O1 and non-O1), wound and soft tissue infections (non-O1), local and generalised sepsis (non-O1), bacteraemia and septicemia (non-O1 strains in cirrhosis and leukemia), fulminating systemic infection (non-O1 strains); obligate parasite of man; noninvasive intestinal infection; O1 strains cause epidemics; epidemic strains divided into classical and eltor biovars on basis of haemolysis of sheep erythrocytes, VP reaction, haemagglutination of chicken erythrocytes, susceptibility to polymyxin and phage typing; subdivision into biovars not supported by hybridisation studies; eltor biovar causes less explosive outbreaks and is more resistant to environmental conditions; oral disease-producing dose in man 10^9 bacteria, 10^4 + bicarbonate; attaches to epithelium of small intestine (receptor is fucose and mannose), rarely penetrates, and causes diarrhoea by forming an enterotoxin (choleragen) which activates adenyl cyclase, raising CAMP level in intestinal epithelial cells, causing water and electrolyte loss from epithelial cells into intestine; transmitted by food and water (viability from 1 d in beer, cola drinks and carbonated water to 60 d in sea water at 5-10°C); short-lived immunity to infection following attack of cholera is most likely mediated by antitoxin; treatment: rehydration and electrolyte replacement, doxycycline, tetracycline (usually susceptible), cotrimoxazole (usually susceptible), norfloxacin (usually susceptible), erythromycin, furazolidone, chloramphenicol (usually susceptible); also susceptible to fleroxacin (MIC $\leq$ 0.06 mg/L), usually susceptible to ampicillin, amoxycillin-clavulanate, trimethoprim, ciprofloxacin, nalidixic acid

V.cincinnatii: motile with a single polar flagellum; requires NaCl for growth (tolerates 6% NaCl); grows on TCBS agar; ferments glucose (no gas) and sucrose; positive test reactions for lysine decarboxylase and ONPG; indophenol oxidase produced; VP reaction positive; negative test reactions for indole, ornithine decarboxylase, arginine dihydrolase and urease; cause of meningitis and septicemia in 1 patient; treatment: moxalactam

V.fluvialis: motile with a single polar flagellum; requires NaCl for growth (tolerant to 6-7% NaCl); grows on MacConkey and TCBS agars; ferments glucose (no gas), sucrose, maltose and mannitol; indophenol oxidase produced; positive test reactions for ONPG and arginine dihydrolase; indole production strain variable; isolated from human wound; causes diarrhoea, gastroenteritis and ileitis following consumption of seafood, rarely wound infections, primary septicemia

V.furnissii: biochemically similar to *V.fluvialis* except for gas production from glucose; causes gastroenteritis

V.harveyi: O/129 partially susceptible

V.metschnikovii: motile with a single polar flagellum; requirement for NaCl strain variable (tolerance to 8% NaCl strain variable); grows on TCBS; ferments glucose (no gas) and sucrose; positive test reactions for arginine dihydrolase, lysine decarboxylase (usually) and VP; ONPG and indole production strain variable; negative test reactions for nitrate and ornithine decarboxylase; gelatine and mannitol positive; urease, melibiose, amygdalin, arabinose and oxidase negative; O/129 susceptible; cause of cholecystitis and associated bacteraemia in 1 patient, isolated from 5 infants with diarrhoea

V.mimicus: motile by a single polar flagellum; NaCl not required for growth (tolerates 3% NaCl); grows on TCBS; ferments glucose (no gas), maltose, lactose (slow) and mannitol, but not sucrose; indophenol oxidase produced; positive test reactions for ONPG, indole, lysine decarboxylase and ornithine decarboxylase; urease, inositol, sorbitol, rhamnose, melibiose and arabinose negative; causes diarrhoea, gastroenteritis and ileitis following consumption of seafood (85% of infections), wound infections, local and generalised sepsis and acute otitis after exposure to sea water; treatment: tetracycline, chloramphenicol

V.natriengens: O/129 partially susceptible

V.parahaemolyticus: motile with a single polar flagellum; requires NaCl for growth (tolerates 8% NaCl); grows on MacConkey and TCBS; ferments glucose (no gas), maltose and mannitol, but not lactose or sucrose (usually); indophenol oxidase produced; positive test reactions for indole, lysine decarboxylase, ornithine decarboxylase and L-arabinose; negative test reactions for ONPG, arginine dihydrolase, inositol, sorbitol, melibiose; O/129 partially susceptible; causes eye infections (panophthalmitis, purulent conjunctivitis), gastroenteritis (food poisoning; acquired from fish, shellfish and processed seafoods (especially from tropical waters, notably East Asia); disease-producing dose 10^5-10^7 organisms; multiplication in intestine; cholera-like enterotoxin; nausea and vomiting, severe abdominal pain and acute watery diarrhoea; incubation period 2-48 h; 59% of infections), puncture wound infections (34% of infections), cellulitis, local and generalised sepsis, primary septicemia (5% of infections; erythema multiforme, haemolytic anaemia, hypotension), localised skin lesions in septicemia and endocarditis, reactive arthritis; treatment: doxycycline + ceftazidime or ciprofloxacin or gentamicin (not required in gastrointestinal infections)

V.vulnificus: motile with a single polar flagellum; requires NaCl for growth (tolerates 6% NaCl); grows on MacConkey and TCBS; ferments glucose (no gas) and lactose (weak or delayed), but not sucrose (usually); indophenol oxidase produced; positive test reactions for ONPG, indole, lysine decarboxylase, ornithine decarboxylase, cellibiose and salicin; arginine dihydrolase not produced; urease, inositol, sorbitol, rhamnose and melibiose; cause of endometritis (woman engaging in sex in sea water), osteomyelitis and osteochondritis (trauma in seawater), pneumonia (in drowning victim), septicemia after ingestion of raw shellfish (major danger for persons with chronic liver disease), soft tissue and wound infections, cellulitis, local and generalised sepsis, rhabdomyolysis after contact with marine environment or handling shellfish; treatment: doxycycline + ceftazidime or ciprofloxacin or gentamicin

Order Xanthomonadales

Family Xanthomonadaceae

Stenotrophomonas maltophilia: colonies develop a characteristic lavender-green colour on blood agar; growth accompanied by a strong smell of ammonia; obligately aerobic; asporogenous; rods, motile by a polar tuft of 1-6 or more flagella; hydrolyses DNA; oxidative (delayed) in glucose, maltose, sucrose, lactose and certain other carbohydrates; positive test reactions for catalase, lysine decarboxylase and for hydrolysis of esculin and gelatine; usually no growth at 42°C or 4°C; nitrate and nitrite reduction negative; starch negative; usually oxidase negative; indole not formed; either methionine or cystine + glycine required for growth; alkaline phosphatase heat sensitive; wide geographic distribution; isolated from water, soil, animal sources, plant material and all varieties of human clinical specimens; occasionally an opportunist associated with urinary tract (acute pyelonephritis associated with hospitalisation and antimicrobial therapy) and respiratory tract infections (pneumonia following hospitalisation and antimicrobial therapy), postoperative and posttraumatic wound infections, endocarditis (associated with i.v. drug abuse and prosthetic valve surgery), bacteraemia and septicemia (nosocomial infections in immunocompromised patients receiving broad spectrum antimicrobials), meningitis, mastoiditis, conjunctivitis, ecthyma gangrenosum, pseudobacteremia; 2% of nosocomial infections (3% of Gram negative bacilli); high incidence of infections in patients with malignant solid tumours, leukemia and lymphoma; susceptible to ticarcillin-clavulanate (98%), cotrimoxazole (2% resistance in hospitals in Australia); 100% intrinsic resistance to ampicillin, amoxycillin, amoxycillin-clavulanate, cephalosporins except ceftazidime (92% susceptible), imipenem and meropenem; 79% intrinsic resistance to aminoglycosides (possibly all resistant in clinical practice), commonly resistant to ticarcillin, piperacillin, azlocillin

Phylum Spirochaetes

Class Spirochaetes

Order Spirochaetales: thin spirals, flexuous, motile but no flagella, Gram negative

Family Brachyspiraceae

Brachyspira pilosicoli: causes diarrhoea in pigs, dogs, birds and humans (especially in developing countries and in HIV patients and homosexual males); also bacteraemia in debilitated patients

Treponema hyodysenteriae: causes swine dysentery, linked to long-standing diarrhoea in humans

Family Leptospiraceae

Leptospira: aerobic, flagellated spirochaete; mostly pathogen of animals; causes leptospirosis (Weil's disease), abortion, adult hepatitis, anterior uveitis, erythema nodosum, non-pyogenic meningitis, rhabdomyolysis; diphasic illness due to disappearance from blood and spinal fluid and appearance of antibody; transmission by contact with water contaminated with urine from infected animals (rats, etc); most important site of survival in epidemiological spread is lumen of convoluted tubules in mammals; carried in blood free in plasma; can be seen by dark field microscopy or antigen stains; treatment: oxytetracycline

L.interrogans: causes leptospirosis; numerous serogroups—icterohaemorrhagicae (30% of total), canicola (25% of total), autumnalis (15% of total), pomona (10% of total), ballina, bataviae, grippotyphosa; diagnosis: phase examination and culture of blood (first week of infection), urine (second and third weeks), serology (complement fixation test for group + microscopic agglutination test for serovars; ELISA); treatment: amoxycillin, penicillin, tetracycline

Family Spirochaetaceae: no muramic acid in cell wall, inactivated by antibody, anaerobic; spirochaetosis is a general term for a disease caused by any bacterium of this family

Borrelia: flagellate spirochaete transmitted to humans by ticks; causes borreliosis; transmission by bite of ticks (worldwide, with major centres in N Africa, Northern India, Russia, Central Asia, S America), lice (Ethiopia major endemic area; also N Africa, W Africa, Namibia, eastern Europe, India, southern USA), infected insect feces, infected rodents; undergoes antigenic shift during infection; infection usually diagnosed by examination of Wright- or Giemsa-stained peripheral blood

'B.america': vector *Ornithodoros alactogalis*; reservoir rodents; America

B.anserina: causes avian borreliosis; vector *Argas*, ? mites; reservoir fowl; worldwide

'B.brasiliensis': vector *Ornithodoros brasiliensis*; Brazil

B.burgdorferi: causes Lyme disease and related disorders (acrodermatitis chronica atrophicans, erythema chronicum migrans, 11% of carpal tunnel syndrome); vector *Ixodes dammini* in Eastern United States, *Ixodes pacificus* in Western United States, *Ixodes ricinus* in Europe, *Ixodes persulcatus* in Asiatic former Soviet Union, China, Japan, ? *Ixodes holocyclus* in Australia, possibly other arthropods worldwide; reservoir rodents, possibly deer and birds; diagnosis: microscopy, isolation, indirect immunofluoresecent antibody, ELISA, haemagglutination, immunoblotting; treatment: tetracycline, penicillin, erythromycin, doxycycline, amoxycillin, ceftriaxone

'B.caucasica': causes Caucasian tick-borne relapsing fever (usually mild endemic); vector *Ornithodoros verrucosus*; reservoir rodents; Caucasus to Iraq; treatment: tetracycline, doxycycline

B.coriaceae: causes epizootic bovine abortion; vector *Ornithodoros coriaceii;* reservoir rodents, ? deer; Western United States; susceptible to ceftriaxone (MIC 0.01-1 mg/L), erythromycin (0.01-1 mg/L), minocycline (0.09-0.17 mg/L), ampicillin (0.25-1 mg/L)

B.crocidurae: causes North African tick-borne relapsing fever (mild); vector *Ornithodoros erraticus* (small variety); reservoir rodents; Morocco, Libya, Egypt, Iran, Turkey, Senegal, Kenya; treatment: tetracycline, doxycycline

B.duttonii: causes East African tick-borne relapsing fever (often severe); vector *Ornithodoros moubatai*; reservoir humans; Central, Eastern, Southern Africa; treatment: tetracycline, doxycycline

'B.graingeri': vector *Ornithodoros graingeri*; Kenya

B.hermsii: causes American tick-borne relapsing fever (often severe); vector *Ornithodoros hermsii*; reservoir rodents, chipmunks, tree squirrels; Western United States; treatment: tetracycline, doxycycline

'B.herveyi': causes tick-borne relapsing fever; treatment: tetracycline, doxycycline

B.hispanica: causes Hispano-African tick-borne relapsing fever (endemic); vector *Ornithdoros erraticus* (large variety); reservoir rodents; Spain, Portugal, Morocco, Algeria, Tunisia; treatment: tetracycline, doxycycline

'B.latysschewii': causes Caucasian tick-borne relapsing fever (usually mild endemic); vector *Ornithodoros tartakovskyi*; reservoir rodents; Iran, Central Asia

'B.mazzottii': causes American tick-borne relapsing fever; vector *Ornithodoros talaje*, ? *Ornithodoros dugesi*; reservoir rodents; Southern United States, Mexico, Central and S America; treatment: tetracycline, doxycycline

'B.merionesi': as for *B.crocidurae*

B.microti: as for *B.crocidurae*

B.parkeri: causes American tick-borne relapsing fever (endemic); vector *Ornithodoros parkeri*; reservoir rodents; Western USA, Canada; treatment: tetracycline, doxycycline

B.persica: causes Asiatic-African tick-borne relapsing fever (endemic); vector *Ornithodoros tholozani*; reservoir rodents; from W China and Kashmir to Iraq and Egypt, former Soviet Union, India; treatment: tetracycline, doxycycline

'B.queenslandica': vector *Ornithodoros gurreyi*; reservoir rodents; Australia

B.recurrentis: causes louse-borne epidemic relapsing fever (vector *Pediculus humanus*; reservoir humans; worldwide, especially Ethiopia, Sudan, S America; ≈ ¼ children; females > males; 40% case-fatality rate untreated, ≈ 5% treated; primary attack duration 6 d, afebrile interval 9 d, 1 relapse), adult hepatitis; carried in blood free in plasma; microbial antigens vary within individual host; treatment: penicillin, tetracycline, erythromycin, chloramphenicol

B.theileri: causes bovine borreliosis; vector *Rhipicephalus, Boophilus*; reservoir cattle, humans, ? sheep; worldwide

'B.tillae': vector *Ornithodoros zumpti*; reservoir rodents; S Africa

B.turicatae: causes American tick-borne relapsing fever (usually mild endemic; most cases young adults and older children; males > females; case-fatality rate < 5%; primary attack duration 4 d, afebrile interval 7 d, 3 relapses); vector *Ornithodoros turicata*; reservoir rodents; Southwestern United States, Central and S America; treatment: tetracycline, doxycycline

'B.venezuelensis': causes tick-borne relapsing fever; treatment: tetracycline, doxycycline

Treponema: helically coiled with axial filaments, very thin, motile, obligately anaerobic, nonsporeforming Gram negative rods; treponematosis is a general term for any disease caused by a bacterium of this genus; ? role in causing necrotising ulcerative gingivostomatitis, balanitis

'T.carateum': causes pinta; treatment: penicillin

T.denticola: ? involved in periodontitis

T.pallidum subsp endemicum: causes nonveneral syphilis

T.pallidum subsp pallidum: obligate human parasite; sexual transmission, transmission in blood; worldwide distribution; related nonvenereal human bacteria; causes venereal syphilis, anterior uveitis (in secondary syphilis), acute epididymitis and epididymoorchitis, hepatic granuloma, adult and prenatal hepatitis, non-pyogenic meningitis (uncommon), prenatal generalised disease, proctitis in AIDS, maculopapular rash, stillbirth; warm, moist skin is more susceptible; attaches to mucopolysaccharide on cell surface or in tissue; mucopolysaccharidase associated with virulence; enters across epithelial surface of urogenital tract and subsequently spreads through body; facultative intracellular; polysaccharide capsular material resists phagocytosis; antibody of poor specificity or affinity fails to neutralise or opsonise; kidney deposits of circulating immune complexes cause glomerulonephritis (nephrotic syndrome in secondary syphilis); persists in disseminated sites (may be infectious, not shed to exterior), causing chronic disease; mean doubling time 30 h in vivo in rabbit; treatment: penicillin (extremely susceptible), tetracycline, erythromycin, doxycycline

T.pallidum subsp pertunue: causes yaws; warm, moist skin is more susceptible; nonvenereal; restricted to tropical areas; extremely susceptible to penicillin

T.refringens: normal flora in mouth

T.vincentii: ? role in causing necrotising ulcerative gingivostomatitis, tropical ulcer; treatment: metronidazole

Unclassified

'Spirillum minus': causes spirillosis (sodoka, sokoshio, spirillar fever, spirillary fever; one type of rat bite fever); diagnosis: isolation by animal inoculation, specific serology not available; treatment: penicillin, tetracycline, erythromycin

Phylum Tenericutes

Class Mollicutes: wall-less procaryotes

Order Acholeplasmatales

Family Acholeplasmataceae: genome size $\approx 10^8$ D; NADH oxidase localised in membrane; sterol not required for growth; all nonpathogenic for man

Acholeplasma: does not require cholesterol; habitat animals, plants, insects; 12 currently recognised species

A.laidlawii: aerobic and anaerobic growth in vitro; glucose positive; arginine and urea negative; coloniser of oropharynx

A.oculi: glucose positive; arginine and urea negative; primary site of colonisation unknown; secondary colonisation/infection of antral fluid

Order Anaeroplasmatales

Family Anaeroplasmataceae

Anaeroplasma: requires cholesterol; obligate anaerobe; habitat bovine and ovine rumen; 4 currently recognised species

Asteroplasma: does not require cholesterol; oxygen sensitive; habitat bovine and ovine rumen; 1 currently recognised species

Order Entomoplasmatales

Family Spiroplasmataceae: helical organisms during some phase of growth; genome size $\approx 10^9$ D; NADH oxidase localised in cytoplasm; sterol required for growth

Spiroplasma: helical filaments; requires cholesterol; habitat arthropods (including insects) and plants; 11 currently recognised species

Order Mycoplasmatales: probably a group of degenerate bacterial forms lacking rigid cell walls (cell wall or cell wall peptidoglycans absent); Gram negative, pleomorphic; visible in optical microscope; filterable through 450 nm pore size filters; contain both RNA and DNA; grow on cell-free media; generate metabolic energy, do not depend on host cells for multiplication, can synthesise proteins by own enzymes, require sterols (except *Acholeplasma*); growth inhibited by antibody alone; growth inhibited by antimicrobials acting on protein synthesis; all resistant to penicillin

Family Mycoplasmataceae: genome size $\approx 5X10^8$ D; NADH oxidase localised to cytoplasm; sterol required for growth

Mycoplasma: small, highly pleomorphic organisms that are difficult to observe with routine smears; cell wall does not contain muramic acid; requires complex medium including cholesterol for growth; does not hydrolyse urea; 88 currently recognised species; habitat man, animals, plants, insects; normal flora of mouth, large intestine, lower ileum, external genitalia, anterior urethra, vagina (13%); causes encephalitis, meningoencephalitis, pneumonia (including diffuse interstitial), ? nonspecific urethritis; inhibits phagocytic ingestion despite attachment; 650 genes; treatment: tetracycline, doxycycline

M.arginini: activates B lymphocyte

M.arthritidis: activates T lymphocyte activation of B cells by superantigen bridge

M.buccale: arginine positive; glucose and urea negative; rare isolates from ororespiratory tract

M.faucium: arginine positive; glucose and urea negative; rare isolates from ororespiratory tract

M.fermentans: glucose and arginine positive; urea negative; rare isolates from lower urogenital tract and oropharynx; secondary colonisation/infection of leukemic bone marrow, arthritic joint, peripheral blood lymphocytes in AIDS, urine in AIDS; activates B and T lymphocytes

M.genitalium: has a flask-shaped appearance, with a specialised terminal portion; exhibits gliding motility; grows slowly, particularly in primary culture; on agar, grows optimally in N_2-5% CO_2 and produces some 'fried egg' colonies; growth inhibited by thallium acetate, tetracycline, erythromycin and other antimicrobials; exhibits haemadsoprtion, reduced by treating erythrocytes with neuraminidase; attaches to cells in tissue and organ cultures and to glass and plastic; has specific proteins, some of which are shared with *M.pneumoniae*; protein of terminal 140 kD portion different from that of *M.pneumoniae* but has considerable sequence homology; is serologically distinct from other *Mycoplasma* species but has some cross-reactivity with *M.pneumoniae* and *M.pirum*; guanine/cytosine ratio 32.4±1 mol%; arginine positive; glucose and urea negative; rare isolates from urogenital tract and oropharynx; secondary colonisation/infection of urethra, synovial fluid in arthritic joint

M.hominis: aerobic and anaerobic growth in vitro; arginine positive; glucose and urea negative; common inhabitant of oropharynx and lower urogenital tract; secondary colonisation/infection of lung and pleural effusion, blood in postpartum septicemia, prostheses, transplants, sites of trauma/surgery, malignancies, CSF, peritoneum, synovial fluid in arthritis, skin, pericardium, amniotic fluid, neonatal septicemia; rarely causes abortional and puerperal infection, 6% of neonatal bacteraemia and septicemia, cellulitis (postcaesarean and others), mucopurulent cervicitis, chorioamnionitis, endometritis, nonpyogenic meningitis, myocarditis and pericarditis, parametritis, pelvic abscess, pelvic inflammatory disease, peritonitis, acute pyelonephritis, salpingitis, septic arthritis associated with prostheses, septicemia in puerperium, ? vaginitis; diagnosis: direct immunofluorescence, culture (identification by growth inhibition, immunofluorescence test, growth agglutination (subspecies)), modified metabolic inhibition, mycoplasmacidal test, indirect haemagglutination; treatment: doxycycline, erythromycin, tetracycline, ciprofloxacin

M.hyorhinis: activates B lymphocytes

M.lipophilum: arginine positive; glucose and urea negative; rare isolates from ororespiratory tract

M.neurolyticum: activates B lymphocytes

M.orale: arginine positive; glucose and urea negative; common inhabitant of ororespiratory tract; secondary colonisation/infection of leukemic bone marrow and of lymph nodes and skin in sarcoidosis; activates B lymphocytes

M.penetrans: glucose and arginine positive; urea negative; coloniser of genital tract; secondary colonisation/infection of urine in male AIDS patients; associated with Kaposi's sarcoma in AIDS

M.pirum: glucose and arginine positive; urea negative; primary site of colonisation unknown; secondary colonisation/infection of peripheral blood lymphocytes

M.pneumoniae: aerobic and anaerobic growth in vitro; glucose positive; arginine and urea negative; haemabsorbs guinea pig red blood cells; rare isolates from ororespiratory tract except during outbreaks of disease; does not colonise but produces acute or subacute infection; primary sites of infection oropharynx, lung, pleural fluid, bronchoalveolar fluid; secondary sites arthritic joints, skin lesions, middle ear fluid, CSF, tubo-ovarian abscess, vagina, pericardial fluid, cardiac blood, kidney, brain; causes acute respiratory illness—pharyngitis/tracheobronchitis (77% of infections; annual rate of 46/1000), acute exudative and nonexudative tonsillitis, acute bronchiolitis and bronchopneumonia, primary atypical pneumonia in children and young adults (usually interstitial; 3% of infections; annual rate 2/1000), pneumonitis in immunodeficient, coryza, bullous myringitis and pleural effusion, ? chronic asthma, also haemolytic anaemia (rare), thrombocytopenia, migratory polyarthritis (rare), hepatitis, myocarditis and/or pericarditis (rare), erythema multiforme, erythema nodosum, nonpyogenic meningitis, encephalitis and meningoencephalitis (rare), macular rash, maculopapular rash, generalised urticarial rash, varicella-like rash, petechial or purpuric rash (rare), ? inflammatory bowel disease; implicated in Stevens-Johnson syndrome and Guillain-Barré syndrome; 20% of infections asymptomatic; 'foot' on surface of organism attaches to neuraminic acid receptor on respiratory epithelial cell; infection generally confined to epithelial surface of respiratory tract; microbial antigens mimic host antigens, leading to poor antibody response; activates B and T lymphocytes; diagnosis: modified metabolic inhibition, cold agglutination (≥ 1:32; sensitivity 50%, specificity 50%), complement fixation test (≥ 1:66; sensitivity 54%, not completely specific), culture on A7B agar (identification by growth inhibition on agar, immunofluorescence); treatment: tetracycline, erythromycin, doxycycline, roxithromycin, minocycline, gatifloxacin, moxifloxacin, azithromycin, clarithromycin

M.primatum: arginine positive; glucose and urea negative; rare isolates from urogenital tract (female urethra); secondary colonisation/infection of umbilicus

M.pulmonis: activates B and T lymphocytes

M.salivarium: arginine positive; glucose and urea negative; common inhabitant of ororespiratory tract; secondary colonisation/infection of cervix/vagina, arthritic joint

M.spermatophilum: arginine positive; glucose and urea negative; coloniser of genitourinary tract (cervix/sperm)

Ureaplasma: requires cholesterol; urease positive; habitat man and animals; normal flora of vagina (54%); ? causes diffuse interstitial pneumonia

U.urealyticum: isolation medium contains sterol and has a pH of 6; urea positive; glucose and arginine negative; serotype 3 haemabsorbs guinea pig red blood cells; isolated from genitourinary tract and oropharynx (rare); other sites of primary colonisation/infection bronchoalveolar fluid, placenta; causes 30-40% of nongonococcal urethritis, prostatitis, acute cystitis, urinary calculi, chorioamnionitis, endometritis, parametritis, pelvic abscess, pelvic inflammatory disease, pneumonia (including neonatal), septic arthritis in hypogammaglobulinemia, puerperal septicemia, 1% of neonatal bacteraemia and septicemia, myocarditis and pericarditis; sexually transmitted; importance not clear; treatment: erythromycin, minocycline, tetracycline, doxycycline; resistant to ciprofloxacin

Chapter 18

Fungi

Fungi/Metazoa Group
Fungi
Subkingdom Dikarya
Phylum Ascomycota
Ascomycota Incertae Sedis
Family Pseudeurotiaceae
Pseudoeurotium ovale: normal flora of skin; ? causes dandruff; treatment: selenium sulphide shampoo
Mitosporic Ascomycota
Acremonium: causes chronic sinusitis in immunocompromised, peritonitis in continuous ambulatory peritoneal dialysis, systemic infections in abnormal host
Fonsecaea: causes chromoblastomycosis; diagnosis: micro and culture, complement fixation test; treatment: surgery, flucytosine + thiabendazole or amphotericin B, ketoconazole ± flucytosine, itraconazole
F.compacta: causes chromoblastomycosis (Far East)
F.pedrosoi: causes brain and epidural abscess, chromoblastomycosis (Far East)
Helminthosporium: causes systemic infections in abnormal host
Madurella mycetomatis: causes mycetoma
Phoma: causes phaeohyphomycosis
Pleurophoma: causes phaeohyphomycosis
Subphylum Pezizomycotina
Class Dothideomycetes
Subclass Dothideomycetidae
Order Capnodiales
Family Davidiellaceae
Mitosporic Davidiellaceae
Cladosporium cladosporioides: causes systemic infections in abnormal host
Family Piedraiaceae
Piedraia hortae: causes black piedra; diagnosis: micro and culture of nodules on hair shafts; treatment: shaving, sulphur ointment
Order Dothideales
Mitosporic Dothideales
Hortaea werneckii: causes tinea nigra; treatment: amphotericin B
Subclass Pleosporomycetidae
Order Pleosporales
Family Leptosphaeriaceae
Leptosphaeria senegalensis: causes mycetoma
Mitosporic Leptosphaeriaceae
Coniothyrium: causes chronic sinusitis in immunocompromised
Family Lophiostomataceae
Mitosporic Lophiostomataceae
Pyrenochaeta romeroi: causes mycetoma
Family Pleosporaceae
Cochiobolus australiensis: causes peritonitis in continuous ambulatory peritoneal dialysis
C.hawaiiensis: causes brain and epidural abscess, phaeohyphomycosis
C.pallescens
Curvularia pallescens: causes brain and epidural abscess
Curvularia lunata: causes rare cases of endocarditis, brain abscess, skin infections, onychomycosis, keratitis, pneumonia, disseminated disease, mycetoma, allergic bronchopulmonary disease, chronic sinusitis; treatment: debridement, surgery
Mitosporic Cochliobolus
Bipolaris: causes chronic sinusitis in immunocompromised, systemic infections in multiple myeloma, 2 cases of meningoencephalitis in cancer patients; diagnosis: histology and culture of biopsy specimens; treatment: itraconazole, amphotericin B

B.spicifera: causes brain and epidural abscess, peritonitis in continuous ambulatory peritoneal dialysis
Curvularia: saprobic dematiaceous mould residing primarily in soil; causes keratitis and iritis, peritonitis in continuous ambulatory peritoneal dialysis (rare); treatment: natamycin
C.geniculata: causes mycetoma, phaeohyphomycosis
Mitosporic Pleosporaceae
Alternaria: causes chronic eye infections, chronic sinusitis in immunocompromised, keratitis and iritis, local and generalised sepsis, mucosal and visceral infections; treatment: itraconazole, natamycin
A.alternata: causes phaeohyphomycosis; produces tenuazonic acid, alternanol and alternanolmonomethyl ether (mycotoxins) in tomatoes, capsicums, eggplants, sorghum, wheat and related grains
Drechslera: causes endocarditis postsurgery for ventricular septal defect, granulomatous encephalitis, keratitis and iritis, localised skin lesions in neutropenics, nonpyogenic meningitis associated with lymphoma, osteomyelitis and osteochondritis associated with prior surgery
D.biseptata: causes pneumonia in disseminated infections
Exserohilum rostratum: causes chronic sinusitis in immunocompromised, phaeohyphomycosis
Class Eurotiomycetes
Subclass Chaetothyromycetidae
Order Chaetothyriales: black yeasts
Family Herpetotrichiellaceae
Mitosporic Herpetotrichiellaceae
Cladophialophora bantiana: causes brain and epidural abscess, phaeohyphomycosis, systemic infections in abnormal host; susceptible to clotrimazole (MIC 0.4 mg/L)
C.carrionii: causes chromoblastomycosis (Australia, S Africa, Venezuela)
Exophiala dermatitidis: causes systemic infection (pneumonia, brain abscess and epidural abscess in chronic granulomatous disease), phaeohyphomycosis; diagnosis: micro and culture of biopsy; treatment: amphotericin B, flucytosine, ketoconazole, fluconazole
Exophiala jeanselmei: causes mycetoma, 1% of fungal peritonitis in continuous ambulatory peritoneal dialysis, phaeohyphomycosis
E.moniliae: causes phaeohyphomycosis
E.pisciphila: causes phaeohyphomycosis
E.spinifera: causes phaeohyphomycosis, 2% of fungal peritonitis in continuous ambulatory peritoneal dialysis
Rhinocladiella: causes chromoblastomycosis
R.atrovirens: 1 case of brain abscess in HIV infected i.v. drug abuser
Subclass Eurotiomycetidae
Order Eurotiales: green and blue molds
Family Trichocomaceae
Emiricella nidulans: causes mycetoma
Mitosporic Trichocomaceae
Aspergillus: ascomycete; dust, soil; most common laboratory contaminant; causes adult hepatitis, arteritis, brain and epidural abscess in neutropenics, chorioretinitis, encephalitis, endocarditis (coronary artery surgery, liver transplantation), endophthalmitis (rare, bloodborne), enterocolitis, hepatic granuloma, keratitis and iritis, localised skin lesions, local and generalised sepsis, lymph gland infections (rare), mycotic aneurism, nonpyogenic meningitis (infrequent in neutropenics and impaired cell-mediated immunity), 1% of nosocomial fungal infections, osteomyelitis (predisposing factors), pericarditis (in 4% of disseminated cases), pneumonia, postseptal cellulitis in immunosuppressed, prostatitis and seminal vesiculitis (uncommon), upper airways infection, urinary infection, vascular graft infection (rare), superinfection in anti-tumour therapy, chronic granulomatous disease, corticosteroid therapy, leukemia during therapy, rheumatoid lung, interrupted integument, neutrophil dysfunction, systemic infection in granulocytopenia, microbicidal abnormality; primary bodily defence mechanism humoral immune responses (phagocytes +++, basophil-mast cell +); deficiencies in neutrophils, mononuclear phagocytes, integument, ? altered normal flora, ? humoral factors in infection; diagnosis: latex agglutination ($\geq$ 1+; anti-culture filtrate antigen), counterimmunoelectrophoresis, immunodiffusion (1-2 bands in aspergilloma/allergy, $\geq$ 3 bands in aspergilloma/invasive aspergillosis), complement fixation test ($\geq$ 1:8; limited value), ELISA, indirect fluorescent antibody (titre $\geq$ 1:66), radioimmunoassay, precipitin, wet preparation, tissue stains (Grocott's methenamine silver, periodic acid-Schiff), culture; treatment: amphotericin B (MIC 0.05-8 mg/L), flucytosine (0.2-1.56 mg/L), itraconazole, natamycin, rifampicin; resistant to miconazole, ketoconazole, fluconazole
A.carbonarius: some isolates produce ochratoxin (grapes and grape products, peanuts)
A.clavatus: causes bagassosis and farmer's lung
A.flavus: uni- or biserrate, conidiophore length 400-850μm, rough-walled, hyphae colourless, vesicle elongate, becoming subspherical to spherical, conidial head radiate, becoming columnar with age, conidia spherical, echinulate, 3-6 μm; colonies

yellow to yellowish-green; produces aflatoxin B (potent hepatocarcinogen), cyclopiazonic acid (nuts, oilseeds, spices, stored commodities; worldwide); causes aspergillosis, endocarditis, otitis externa, 1% of peritonitis in continuous ambulatory peritoneal dialysis, pneumonia (especially in leukemia), chronic sinusitis, thyroiditis, systemic infections in abnormal host; treatment: amphotericin B ± flucytosine or rifampicin, itraconazole

A.fumigatus: uniseriate, conidiophores length up to 320 μm, smooth-walled, greenish coloured hyphae, vesicle dome-shaped, conidial head compact and columnar, conidia spherical to subspherical, echinulate, 2.5-3 μm diameter; colonies whitish green to grey-green; produces exotoxin, proteinases, oxidoreductases; causes 75% of aspergillosis, endocarditis, otitis externa (including rare malignant), 1% of peritonitis in continuous ambulatory peritoneal dialysis, pneumonia (especially in leukemia), thyroiditis, systemic infections in abnormal host; susceptible to interferon-γ and tissue necrosis factor-stimulated macrophages; treatment: amphotericin B ± flucytosine or rifampicin, itraconazole

***A.glaucus*:** causes aspergillosis, systemic infections in abnormal host

A.niger: biserrate; conidiophore length 1.5-3 mm, smooth-walled, colourless or brownish, vesicle spherical, conidial head radiate, conidia spherical, brown/black, roughened, 4-5 μm; colonies white/yellow, developing a black mat of conidia; causes otitis externa; some isolates produce ochratoxin (sun-dried fruit, peanuts)

A.ochraceus: produces ochratoxin in coffee beans

A.parasiticus: produces aflatoxins B and G in peanuts, corn and cottonseed (less widely distributed than *A.fumigatus*)

A.terreus: biserrate, conidiophore length 100-250 μm, smooth-walled, colourless, vesicle hemispherical or dome shaped, conidial head long/columnar, conidia spherical to elliptical, smooth-walled, 2-2.5 μm; causes aspergillosis

A.ustus: primary cutaneous aspergillosis following reduced intensity stem cell transplantation

Penicillium: causes bagassosis and farmer's lung, pneumonia in cancer patients, systemic infections in abnormal host; diagnosis: Grocott methenamine silver, PAS and Wright's stain and culture; treatment: amphotericin B, itraconazole, flucytosine, ketoconazole

P.citrinum: most widespread species in tropics; most common species in flour; produces citrinin (mycotoxin)

P.commune: produces cyclopiazonic acid (mycotoxin) in cheese

P.crustosum: produces penitrem A (mycotoxin) in wide range of processed foods

P.expansum: produces patulin and citrinin (mycotoxins) in pome fruits, grapes, tomatoes, refrigerated foods

P.marneffei: causes infections in T helper lymphocyte deficiency, penicilliosis in AIDS in S E Asia

P.verrucosum: produces ochratoxin A in processed meats and stored grains

Neosartorya: resembles *Aspergillus fumigatus* in conidial state but colonies may remain white

N.fischeri: 2 cases of systemic infection in transplant patients, single case of mixed pulmonary infection in patient with myeloma

N.hiratsukae: reticulated ascospores growing restrictedly on Czapek agar; isolated from air, pasteurised aloe juice and cerebral infection; resistant to amphotericin B, flucytosine; susceptible to itraconazole

N.pseudofischeri: ascospore walls ornamented with raised flaps of tissue resembling triangular projections or long ridge lines; causes localised and invasive infections

Order Onygenales

Family Ajellomycetaceae

Ajellomyces dermatitidis: soil fungus in the Americas; perfect stage yeast forms 2-5 μm (small form) or 8-15 μm, broad-based buds; spherical or oval forms immature spherules, free endospores, nonbudding cells; white, beige, greyish-white colonies; hyphae ± small lateral conidia, conversion to broad-based budding yeasts at 37°C; causes blastomycosis (systemic infection in man), endophthalmitis (bloodborne), enterocolitis, hepatic granuloma, localised skin lesions, 3% of lymph gland infections, splenic abscess (rare), systemic infections in abnormal host (rare cases in haematological malignancy during therapy, impaired cell-mediated immunity, T cell deficiency); enters across epithelial surface of intestinal tract and subsequently spreads through body; produces endotoxin; diagnosis: immunodiffusion (1 band or (more specific) 2 bands), complement fixation test (≥ 1:8; limited value), wet preparation, tissue stains (Grocott's methenamine silver, periodic acid-Schiff), culture, DNA probe, skin tests, ELISA, radioimmunoassay; treatment: amphotericin B (MIC 0.05-0.2 mg/L), ketoconazole, hydroxystilbamidine isethionate, miconazole, fluconazole, itraconazole

Histoplasma capsulatum var capsulatum: yeast form 2-5 μm; spherical or oval forms immature spherules, free endospores, nonbudding cells; white, beige, greyish-white colonies; hyphae ± microconidia and/or tuberculate macroconidia, conversion to small yeasts at 37°C; soil fungus in the Americas, especially Mississippi River Valley in United States; can give lung lesions and systemic illness in man; causes adult hepatitis, anterior uveitis, bone marrow infection, 5% of carpal tunnel syndrome, chorioretinitis, chronic and subacute fever, cutaneous lesions, encephalitis, endocarditis, endophthalmitis (bloodborne), enterocolitis, hepatic granuloma, 27% of lymph gland infections, nonpyogenic meningitis, oronasospharyngeal lesions, pneumonia (including diffuse interstitial), pulmonary histoplasmosis with exanthem, systemic infections in abnormal host (infrequent cases in haematological malignancy, T helper lymphocyte dysfunction); enters across respiratory tract epithelial surface and subsequently spreads through body; inhibits lysosome-phagosome fusion; primary bodily defence

mechanism cellular immune responses (delayed type hypersensitivity activated macrophage +++); dissemination often by reactivation; deficiencies in mononuclear phagocytes, ? humoral factors in infection; interferon-γ, tissue necrosis factor active in experimental infections; diagnosis: latex agglutination ($\geq$ 1:16; anti-histoplasmin antigen), immunodiffusion ('h' band = active histoplasmosis; 'm' band = acute or chronic histoplasmosis or normal skin test positive individual), complement fixation test (anti-whole yeast antigen, anti-histoplasmin; $\geq$ 1:8), Giemsa stain, tissue stains (Grocott's methenamine silver, periodic acid-Schiff), culture, DNA probe; treatment: amphotericin B, flucytosine, ketoconazole, fluconazole, miconazole, itraconazole, cotrimoxazole

H.capsulatum var duboisi: yeast forms 8-15 μm, narrow-based buds; causes histoplasmosis, systemic infections in abnormal host

Family Arthrodermataceae: dermatophytes; skin fungi; cause ringworm, infection of skin, hair and nails; some species acquired from animals; mean doubling time 1-24 h in vitro at 28°C

Arthroderma behamiae: *Trichophyton mentagrophytes*

Trichophyton erinacei: 0.3% of dermatophytes identified in Australia (scalp, body)

T. interdigitale: downy variety; 11% of dermatophytes identified in Australia (mainly foot, body, nail); anthropophilic; causes tinea pedis ('athlete's foot'; 39% of isolations in Australia), tinea unguium, tinea cruris (5% of isolations in Australia)

Arthroderma cajetani: macroconidia abundant, oval to elliptical, thick-walled, verrucose, multi-septate; found in 55% of soils; 0.05% of dermatophytes identified in Australia (solely from foot); produces penicillin and other antibiotics

A.fulvum: macroconidia longer and more clavate than those of *M.gypseum*, 3-6 septa; geophilic; causes sporadic tinea corporis, tinea capitis, tinea barbae

A.gypseum

Microsporum gypseum: macroconidia abundant, ellipsoidal, thin-walled, verrucose, 4-6 celled; found in 68% of soils; 2% of dermatophytes identified in Australia (mainly body and limb); slight decline in relative importance over past 25 y; causes ringworm of scalp (suppuration and kerion common; relatively rare in USA, common in S America, 11% in Queensland) and glabrous skin; produces fusidic acid-like antibiotic, penicillin and other antibiotics

Arthroderma obtusum: zoophilic (pigs) and geophilic; 0.05% of dermatophytes identified in Australia (solely body)

Arthroderma uncinatum: found in 30% of soils

Mitosporic Arthrodermataceae

Epidermophyton: dermatophyte; causes ringworm, infection of skin and nails (never hair)

E.floccosum: normal flora of skin; anthropophilic; ubiquitous but more common in tropics; 9% of dermatophytes identified in Australia (mainly groin, body, foot, limb); causes athlete's foot, skin and nail infections, tinea corporis, tinea cruris (classic eczema marginata; 29% of isolations in Australia), tinea pedis (minority of cases); produces penicillin, actinomycin and other antibiotics

Microsporum: dermatophyte; produces fluorescence with Wood's UV light; causes infection of skin, hair and nails, ringworm; some species acquired from animals

M.audouinii: anthropophilic; 0.05% of dermatophytes identified in Australia (solely from body); causes childhood epidemic tinea capitis (not in Europe, declining importance in USA), systemic infections in abnormal host

M.canis: zoophilic (dogs, cats); 7% of dermatophytes identified in Australia (mainly body, limb, scalp); large decline in relative importance over past 25 y; causes ringworm, nonepidemic scalp infections (ectothrix; uncommon in Europe, $\approx$ 50% in USA, 24% in Australia, 75% in Queensland)

M.ferrugineum: causes ringworm of scalp and glabrous skin; Africa, India, China, Japan

M.gallinae: zoophilic (birds); produces antibiotics

Trichophyton: normal flora of skin; causes athlete's foot, ringworm, skin diseases; infection restricted to skin, nails, hair; some species acquired from animals; produces 'antibacterial substances' (myosine, ? penicillin); susceptible to clotrimazole (MIC < 0.05-1.56 mg/L)

T.concentricum: 0.05% of dermatophytes identified in Australia (body only)

T.equinum: some strains require nicotinic acid (not most Australian strains—*T.equinum var autotrophicus*); zoophilic (horses); 0.05% of dermatophytes identified in Australia

T.mentagrophytes: perfect state *Arthroderma benhameii*; urease positive in 2-5 d, red pigment not formed; found in 4% of soils; declining relative importance in Australia over past 25 y; produces penicillin and 6-aminopenicillanic acid

T.mentagrophytes var granulosum: 8% of dermatophytes identified in Australia (mainly foot, body, limb, hand, face); zoophilic (rodents); causes ringworm of smooth skin, suppurative folliculitis in scalp and beard

T.mentagrophytes var interdigitale: downy variety; 11% of dermatophytes identified in Australia (mainly foot, body, nail); anthropophilic; causes tinea pedis ('athlete's foot'; 39% of isolations in Australia), tinea unguium, tinea cruris (5% of isolations in Australia)

T.rubrum: produces red pigment on lactrimel and T1 medium in 2 w, urease negative at 1 w; anthropophilic; 53% of dermatophytes identified in Australia (all sites; most commonly body and foot, rarely scalp; large increase in relative importance over past 25 y); causes tinea cruris (63% of isolations in Australia), tinea pedis (53% of isolations in Australia),

tinea unguium (most common cause in USA; 74% of isolations in Australia), psoriasis-like lesions of smooth skin (25% of tinea corporis), mild suppurative folliculitis in beard; produces penicillin and other antibiotics
T.schoenleini: anthropophilic; causes favus in scalp and smooth skin, scutulum and kerion; Europe, Far East, rare in USA
T.soudanense: 0.05% of dermatophytes identified in Australia (body only); causes more inflammatory types of tinea capitis and tinea corporis; Central and W Africa
T.terrestre: perfect state *Arthroderma quadrifolium*; geophilic; 0.7% of dermatophytes identified in Australia (all sites except scalp, face); produces penicillin and other antibiotics
T.tonsurans: slow growing, growth enhanced by thiamine; anthropophilic; 7% of dermatophytes identified in Australia (mainly body, scalp (46% of isolations in Australia, 11% in Queensland), limb and face); causes black dot ringworm of scalp and smooth skin, sycosis, onychomycosis in all age groups; common in Aborigines and in slums; causes 95% of tinea capitis in USA
T.verrucosum: growth stimulated by inositol and (to much lesser extent) by thiamine; zoophilic (cattle); 0.9% of dermatophytes identified in Australia (limb, body, face, hand; slight decline in relative importance over past 25 y); causes nonepidemic ringworm of scalp and smooth skin, suppurative folliculitis in scalp and beard; produces penicillin and other antibiotics
T.violaceum: growth stimulated by thiamine; anthropophilic; 0.7% of dermatophytes identified in Australia (scalp, body, nail, groin, hand; slight decline in relative importance over past 25 years); causes black dot endothrix infections in scalp and smooth skin (kerion frequent), onychomycosis; common in Europe and Far East, rare in USA
Mitosporic Onygenales
Chrysosporium: causes chronic sinusitis in immunocompromised, endocarditis associated with prostheses, 1% of peritonitis in continuous ambulatory peritoneal dialysis
Coccidioides immitis: spherical or oval forms immature spherules, free endospores, nonbudding cells; white, beige, greyish-white colonies; hyphae ± alternate, doliiform arthroconidia, conversion to endosporulating spherules in vivo; Southwest North America, Central America, northern South America; 40% of infections symptomatic; 85% of these mild, influenza-like illness, 8% severe pulmonary disease, 7% disseminated extrapulmonary disease; causes encephalitis, endophthalmitis (bloodborne), enterocolitis, erythema nodosum, hepatic granuloma, 2% of lymph gland infections, nonpyogenic meningitis, pneumonia (including diffuse interstitial) with exanthem, systemic infections in abnormal host (< 1% of total cases; infrequent cases in haematological malignancy during therapy, T helper lymphocyte dysfunction, second half of pregnancy and postparatum, steroid use, HIV infection); produces proteinases; immunity cell-mediated (delayed type hypersensitivity-activated macrophage +++), basophil-mast cell (+); dissemination often by reactivation; deficiencies in mononuclear phagocytes, ? humoral factors in infection; susceptible to interferon-γ and tissue necrosis factor-stimulated macrophages; diagnosis: latex agglutination (anti-culture filtrate antigen; IgM), immunodiffusion tube precipitin (IgM), immunodiffusion complement fixation test (IgG), counterimmunoelectrophoresis, complement fixation test (≥ 1:8; limited value), coccidioidin skin test, wet preparation, tissue stains (Grocott's methenamine silver, periodic acid-Schiff), culture (may be pigmented, may fail to produce arthroconidia, identify by exoantigen test (F, HL, HS) or spherule production in guinea pig testis) of appropriate specimens from affected tissues or fluid from these tissues, DNA probe; treatment: amphotericin B, miconazole, ketoconazole, fluconazole, itraconazole; also susceptible to clotrimazole (MIC 0.05-0.1 mg/L)
Paracoccidioides brasiliensis: causes paracoccidioidosis, enterocolitis, systemic infections in abnormal host (impaired cell-mediated immunity); growth stimulated by excess iron; treatment: ketoconazole, sulphonamides, amphotericin B, miconazole, fluconazole, itraconazole
Class Orbiolomycetes
Order Orbiliales
Family Orbiliaceae
Mitosporic Orbiliaceae
Dactylaria: causes brain and epidural abscess
Class Sordariomycetes
Sublass Hypocreomycetidae
Order Hypocreales
Family Clavicipitaceae
Mitosporic Clavicipitaceae
Paecilomyces lilacinus: causes chronic sinusitis in immunocompromised
Family Hyocreaceae
Mitosporic Hypocreaceae
Trichoderma: resistant to most antifungal agents
T.longibrachiatum: causes peritonitis in continuous ambulatory peritoneal dialysis, invasive infections in immunocompromised patients
T.viride: causes peritonitis in continuous ambulatory peritoneal dialysis

Mitosporic Hypocreales

Fusarium: causes chronic eye infections, fungemia, keratitis and iritis, 5% of fungal peritonitis in continuous ambulatory peritoneal dialysis, systemic infections in abnormal host (rare cases in burns, haematological malignancy, interrupted integument, neutropenia); diagnosis: histology and culture; treatment: natamycin, granulocyte infusions, GM-CSF

F.chlamydosporum: causes fusariosis

F.falciforme: causes mycetoma

F.oxysporum: causes fusariosis; produces moniliformin (mycotoxin) on processed foods

F.solani: causes fusariosis

Family Nectriaceae

Gibberella

***Gibberella fujikuroi* Complex**

Gibberella fujikuroi: causes fusariosis; produces fumonisins (mycotoxins) on maize

G.intermedia: causes fusariosis

Mitosporic *Gibberella fujikuroi* Complex

Fusarium anthophilum: causes fusariosis

Gibberella zeae: produces trichothecenes and zearalenone (mycotoxins) on wheat and corn

Order Microascales

Family Microascaceae

Microsporic Microascaceae

Scedosporium: causes cellulitis (posttraumatic), osteomyelitis and osteochondritis (penetrating injury, surgery), otitis externa; diagnosis: micro and culture of appropriate specimen; treatment: debridement, itraconazole

S.prolificans: causes chronic sinusitis in immunocompromised, pneumonia in disseminated infection; resistant to amphotericin B

Pseudallescheria boydii: perfect stage of *Scedosporium apiospermum*; causes brain and epididymal abscess in malignant lymphoma and immunosuppression, chronic eye infections, chronic sinusitis, endocarditis in prosthetic valves and in AIDS, endophthalmitis in immunosuppressed, local and generalised sepsis in cancer patients, meningitis (uncommon), mycetoma, pneumonia in disseminated infections, systemic infections in abnormal host (in chronic pulmonary disease, haematological malignancy during therapy, neutrophil dysfunction); diagnosis: immunodiffusion (4-5 bands), wet preparation, Grocott's methenamine silver stain, culture; treatment: ketoconazole, fluconazole, flucytosine; also susceptible to miconazole; resistant to amphotericin B

Sordariomycetes Incertae Sedis

Order Calosphaeriales

Family Calosphaeriaceae

Mitosporic Calosphaeriaceae

Phaeoacremonium parasiticum: causes phaeohyphomycosis

Pleurostomophora repens: causes phaeohyphomycosis

P.richardsiae: causes phaeohyphomycosis

Family Magnaporthaceae

Mitosporic Magnathoraceae

Phialophera verrucosa: causes chromoblastomycosis, phaeohyphomycosis

Subclass Sordariomycetidae

Order Ophiostomatales

Family Ophiostomataceae

Mitosporic Ophiostomataceae

Sporothrix schenckii: mycelial form on standard media at 25°C, yeast forms on blood glucose cysteine agar or in brain heart infusion broth; causes sporotrichosis (cutaneous lymphatic, fixed cutaneous, localised extracutaneous, disseminated), 5% of carpal tunnel syndrome, endophthalmitis (bloodborne), enterocolitis, 1% of lymph gland infection, pneumonia, systemic infections in abnormal host (rare cases in haematological malignancy during therapy); treatment: amphotericin B, ketoconazole, itraconazole, potassium iodide

Subphylum Saccharomycotina

Class Saccharomycetes

Order Saccharomycetales: budding yeasts

Family Dipodascaceae

Dipodascus capitatus: causes systemic infections in leukemia; diagnosis: blood cultures, smear and culture of sputum, sinus, biopsy; treatment: amphotericin B + flucytosine

Galactomyces

Geotrichum candidum: reproduction by arthrospores only, forms a true mycelium; causes chronic sinusitis in immunocompromised, disseminated infections in cancer patients, pneumonia in disseminated infections, systemic infections in abnormal host; diagnosis: micro and culture of sputum, pus from oral lesions, faeces; treatment: amphotericin B

Family Metschnikowiaceae

Clavispora lusitaniae: cellobiose fermented, rhamnose assimilated; causes 1% of catheter associated fungemia and fungal septicemia, chronic and subacute fever in immunocompromised, urinary tract infection in diabetics, vasculitis in immunocompromised; treatment: amphotericin B + flucytosine, fluconazole

Mitosporic Saccharomycetales

Candida: reproduction by pinched blastospores, may form pseudomycelium or true mycelium, no capsule or carotenoid pigment; urea usually negative, does not utilise inositol; normal flora of vagina (13%), skin, upper respiratory tract; causes candidiasis (worldwide; mucocutaneous—predisposing conditions diabetes mellitus, oral contraceptives, broad spectrum antibiotics—and systemic—predisposing conditions neutropenia, parenteral nutrition, ambulatory peritoneal dialysis, heroin addiction, corticosteroids), septic arthritis, balanitis, bagassosis and farmer's lung, cholangitis and cholecystitis (uncommon; in AIDS), chorioretinitis, purulent conjunctivitis, acute empyema, endocarditis, enterocolitis, adult hepatitis, hepatic granuloma, localised skin lesions in disseminated infections, postneonatal pyogenic and nonpyogenic meningitis, myocarditis and pericarditis (cardiac surgery, impaired host defences, severe debilitating disease), oesophagitis, osteomyelitis (drug abusers, periprosthetic), parametritis, pelvic abscess, pelvic inflammatory disease (associated with suture, IUD), peritonitis in chronic peritoneal dialysis, pneumonia (including diffuse interstitial), prenatal generalised disease, prostatic abscess (catheterised diabetics receiving broad spectrum antibiotics), 1-4% of septicemia, 8% of thrombophlebitis, thyroiditis, urethritis (uncommon in male), vaginitis, infections in abnormal host (interrupted integument, infusion infection, surgical procedure, neutrophil dysfunction, T helper lymphocyte dysfunction), superinfection in DiGeorge's syndrome, haematological malignancy during therapy, hypoadrenalism, hypoparathyroidism, hypothyroidism and thymic dysplasia, 72% of nosocomial fungal infections (traumatised skin, i.v. drug abuse, malnutrition, neutropenia, impaired cell-mediated immunity), systemic infection in chemotaxis defect, granulocytopenia, microbial abnormality; intravenous and bladder catheters, altered normal flora by antibiotics, deficiencies in integument, neutrophils, mononuclear phagocytes, ? humoral factors in infection; immunity due to phagocytes (++), alternative complement (+), immune adherence (phagocytosis; ++), basophil (+) in systemic infection, cell-mediated (delayed type hypersensitivity-activated macrophage +++) in chronic mucocutaneous; recovery from primary infection due to antibody, ? cell-mediated immunity; diagnosis: precipitation test, agglutination ($\geq$ 1:16; anti-yeast cell antigen), immunodiffusion (antimannan antigen), counterimmunoelectrophoresis (anti-non-mannan antigen), indirect fluorescent antibody (titre $\geq$ 1:66), ELISA (antigen, antibody), latex agglutination, radioimmunoassay, indirect haemagglutination assay, wet preparation, tissue stains (Grocott's methenamine silver, periodic acid-Schiff), culture; treatment: amphotericin B (MIC 0.2-1.56 mg/L), clotrimazole, fluconazole, itraconazole, ketoconazole, miconazole, nystatin, candicidin, flucytosine

C.albicans: germ tube positive; normal flora of mouth, throat, colon, lower ileum, external genitalia (adherence to labium majus +), anterior urethra, vagina, skin; causes candidiasis (moniliasis)—51% of fungemia and fungal septicemia, balanoposthitis, bronchitis, mucopurulent cervicitis, purulent conjunctivitis, acute cystitis, chronic dacrocystitis, adenitis and canaliculitis, dermatitis, endocarditis, endophthalmitis, chronic eye infections, chronic and subacute fever, local and generalised sepsis, meningitis, 58% of fungal nosocomial infections, 3% of otitis externa, paronychia, perianal and perirectal abscess in patients with malignant disease, perinatal generalised disease, perinephric abscess, 42% of fungal peritonitis in chronic peritoneal dialysis, nonexudative pharyngitis and tonsillitis, pneumonitis, postoperative complications, prostatitis and seminal vesiculitis (uncommon), pulmonary infections, septic arthritis, systemic infections in abnormal host (all organs; common; chronic granumolatous disease), thrush, 5% of tinea pedis, vaginitis (common), vulvitis, vulvovaginitis; can be sexually transmitted; infection generally confined to epithelial surface of respiratory tract, conjunctiva and urogenital tract; produces endotoxin, proteinases, phospholipases, lysophospholipases; growth stimulated by excess iron; primary bodily defence mechanism cellular immune responses, leucocyte bactericidal function; susceptible to interleukin-3, interleukin-4, granulocyte macrophage colony stimulatory factor and macrophage stimulatory factor-stimulated macrophages; interleukin-1, granulocyte colony stimulatory factor and tissue necrosis factor also induce antimicrobial activity; interferon-γ active in experimental infections; mean doubling time 30 minutes in vitro at 37°C; treatment: amphotericin B (MIC 0.2-0.78 mg/L), nystatin, natamycin, gentian violet, clotrimazole, ketoconazole (0.008 mg/L), itraconazole (0.02 mg/L), miconazole (0.17 mg/L), fluconazole (0.39 mg/L), flucytosine, econazole

C.albincas var stellatoideae: causes purulent conjunctivitis (infrequent to rare); treatment: amphotericin B + flucytosine

C.dubliniensis: germ tube and chlamydospore positive, β-glucosidase negative, very weak growth at 42°C, no growth at 45°C; causes oral candidiasis and candidemia

C.glabrata: normal flora of mouth, female genital tract (low numbers); causes septic arthritis in prostheses, purulent conjunctivitis (infrequent to rare), 7% of nosocomial fungal infections, 2% of fungal peritonitis in continuous ambulatory peritoneal dialysis, psoas abscess, systemic infections (fungemia (13% of fungal isolates), urinary tract infections) in

abnormal host (in diabetes mellitus, haematological malignancy during therapy, traumatised skin, chronic granulomatous disease, solid tumours), vaginitis (rare); diagnosis: agglutination, immunodiffusion (cross-reaction with *Candida*), wet preparation, Grocott's methenamine silver stain, culture; treatment: amphotericin B (MIC 0.1-0.4 mg/L), clotrimazole, boric acid, flucytosine

C.kruisii: causes 9% of fungemia and fungal septicemia, endocarditis (rare), 1% of fungal peritonitis in chronic peritoneal dialysis; treatment: amphotericin B ± flucytosine; also susceptible to miconazole, ketoconazole, itraconazole; resistant to fluconazole

C.parapsilosis: trehalose not fermented; causes 6% of fungemia and fungal septicemia, onchomycosis (rare), 8% of fungal peritonitis in continuous ambulatory peritoneal dialysis, purulent conjunctivitis (infrequent to rare), septic arthritis in prostheses, systemic infections in abnormal host (endocarditis (in i.v. drug addicts, invasive procedure, prosthetic devices, hyperalimentation), fungemia); produces proteinases; susceptible to interferon-γ-activated macrophages; treatment: amphotericin B ± flucytosine, fluconazole, ketoconazole, miconazole

C.tropicalis: soluble starch assimilated, maltose fermented; causes 13% of fungemia and fungal septicemia, 14% of fungal peritonitis in continuous ambulatory peritoneal dialysis, psoas abscess, purulent conjunctivitis (infrequent to rare), septic arthritis, systemic infections in abnormal host (endocarditis, peritonitis), vaginitis (rare); produces proteinases; treatment: amphotericin B ± flucytosine, fluconazole, itraconazole; resistant to ketoconazole

Family Saccharomycetaceae

Kluyveromyces marxianus: causes disseminated candidiasis (rare), 1% of catheter associated fungemia and fungal septicemia; treatment: amphotericin B ± flucytosine, fluconazole

Pichia: causes fungemia in cancer patients; treatment: amphotericin B ± flucytosine, fluconazole

Hansenula anomala: causes systemic infections in immunosuppression, use of intravenous devices, previous treatment with antibacterial drugs; diagnosis: blood cultures, histology and culture of biopsy specimens; treatment: amphotericin B

Pichia angusta: causes systemic infections

Pichia guilliermondii: causes 6% of fungemia and fungal septicemia (1% of catheter associated), 3% of fungal peritonitis in chronic peritoneal dialysis, systemic infections in abnormal host (endocarditis, joint infections); treatment: amphotericin B ± flucytosine, fluconazole

Saccharomyces boulardii: prevents antimicrobial-associated colitis; may cause fungemia in critically ill patients

S.cerevisiae: 6000 genes; raffinose assimilated; 1% of catheter associated fungemia in cancer patients, invasive infections, vaginitis (rare); treatment: clotrimazole, boric acid, ketoconazole, amphotericin B ± flucytosine, fluconazole

Subphylum Taphrinomycotina

Class Pneumocystidiomycetes

Order Pneumocystidales

Family Pneumocystidaceae

Pneumocystis: previously classified as parasite; causes pneumonia (interstitial plasma cell pneumonia, plasma cell pneumonia of infants); growth stimulated by excess iron

P.jiroveci: causes acute diarrhoea and/or vomiting in AIDS, diffuse interstitial plasma cell pneumonia, disseminated infection (AIDS, haematological malignancy, lymphoreticular malignancy, immunosuppressive therapy), systemic infection in cell-mediated immunity disorders; primary bodily defence mechanism humoral immune responses (immune adherence (phagocytosis) +++); resistance to reactivation of latent infection due to cell-mediated immunity (delayed type hypersensitivity-activated macrophage +++); interferon-γ, tissue necrosis factor and interleukin-1 active in experimental infections; diagnostic stage in lung; diagnosis: indirect fluorescent antibody (titre ≥ 1:40), toluidine blue O stain of transtracheal aspirate, brush biopsy or open lung biopsy, Grocott's methenamine silver tissue stain, culture in Vero cells; treatment: miconazole, chloroquine, cotrimoxazole, pentamidine isethionate, carbutamide, trimethoprim + dapsone, eflornithine, trimetrexate + calcium folinate + sulphadiazine, clindamycin + primaquine; prednisolone for hypoxia

Phylum Basidiomycota

Agaricomycotina

Class Homobasidiomycetes

Subclass Agaricomycetidae

Order Agaricales

Family Schizophyllaceae

Schizophyllum: causes chronic sinusitis in immunocompromised

Class Tremellomycetes

Order Filobasidiales

Family Filobasidiaceae

Filobasidium uniguttulatum: single report of ventriculitis; susceptible to amphotericin B (MIC 0.25 mg/L), itraconazole (1 mg/L)

Mitosporic Filobasidiales

Cryptococcus: unicellular budding cells only, reproduces by blastospores pinched off mother cell, cells surrounded by capsule; most urease positive; growth stimulated by excess iron; starch-like substance produced, no carotenoid pigment, utilises inositol; susceptible to miconazole, ketoconazole, fluconazole, itraconazole

Cryptococcus albidus: rarely causes cryptococcosis

Order Tremellales: jelly fungi

Mitosporic Tremellales

Cryptococcus laurentii: rarely causes cryptococcosis

Family Tremellaceae

Filobasidiella

Filobasidiella/Cryptococcus neoformans species complex

Cryptococcus neoformans: brown colonies on caffeic acid agar; occurs in soil and pigeon faeces; causes cryptococcosis—nonpyogenic meningitis most usual infection, occasionally gives also chronic and subacute fever, encephalitis, hepatic granuloma, skin lesions (rare), pneumonia (diffuse interstitial in T cell deficiency), chronic pneumonitis, chorioretinitis (associated with meningitis), endocarditis, enterocolitis, endophthalmitis (rare, bloodborne), 2% of lymph gland infections, osteomyelitis and osteochonditis, pancreatitis (18% of cases in AIDS), urinary infection, systemic disease in abnormal host (in adrenal hyperplasia, Hodgkin's disease, immunosuppressive therapy, sarcoidosis, T helper lymphocyte dysfunction, chemotactic defect, ? corticosteroid therapy, ? diabetes mellitus); enters across respiratory tract epithelial surface and subsequently spreads through body; ? dissemination to CNS by reactivation; deficiencies in mononuclear phagocytes, integument, ? humoral factors in infection; polysaccharide capsule (polymer containing uronic acid) resists phagocytosis (virulence factor); multiplies in macrophages; produces proteinases (possible virulence factor); melanin synthesis, growth at 37°C, myristoylation and urease other virulence factors (possibly also matα, mannitol synthesis, phospholipase, signal transduction via calcineurin); immunity cell mediated (delayed type hypersensitivity-activated macrophage +++), phagocytes (++), alternative complement (+), antibody-dependent cellular cytotoxicity (+++); susceptible to macrophage colony stimulatory factor-stimulated macrophages; interferon-γ active in experimental infections; diagnosis: latex agglutination (antipolysaccharide capsular antigen; negative if *C.albidus* infection), tube agglutination, charcoal particle agglutination, indirect fluorescent antibody titre, complement fixation test, India ink preparation, mucicarmine stain, culture; treatment: amphotericin B (MIC 0.05-0.78 mg/L), flucytosine, miconazole, itraconazole, fluconazole; also susceptible to ketoconazole

C.neoformans var neoformans: causes 84% of cryptococcosis in Australia; 70% of cases in immunodeficient

Filobasidiella bacillispora

Cryptococcus gattii: causes 12% of cryptococcosis in Australia; associated with Red Gum trees; most cases in normal hosts

Trichosporon: reproduction by blastospores and arthrospores, mycelium and pseudomycelium formed; causes fungemia, infections in abnormal host (neutrophil dysfunction), pneumonia and disseminated infections in cancer patients; growth stimulated by excess iron; susceptible to amphotericin B (MIC 0.78-3.13 mg/L), ketoconazole, fluconazole, itraconazole

T.beigelii: causes peritonitis in continuous ambulatory peritoneal dialysis (rare), systemic infections in abnormal host; diagnosis: blood cultures, culture and histology of specimens; treatment: amphotericin B + flucytosine

T.cutaneum: causes white piedra, systemic infections in abnormal host (rare cases of endocarditis, fungemia)

Subphylum Pucciniomycotina

Subclass Microbotryomycetes

Order Sporidiobolales

Mitosporic Sporidiobolales

Rhodotorula: unicellular budding forms that may be encapsulated or produce pseudomycelium; carotenoid pigments present; causes infections in abnormal host (interrupted integument)

R.rubra: causes 3% of fungal peritonitis in chronic peritoneal dialysis, systemic infections (fungemia) in abnormal host (cancer patients); treatment: amphotericin B $\pm$ flucytosine, fluconazole

Subphylum Ustilaginomycotina

Ustilaginmycotina Incertae Sedis

Order Malasseziales

Malassezia furfur: causes tinea versicolor (desquamating macular rash), fungemia in patients receiving i.v. fat emulsions; treatment selenium sulphide, sodium thiosulphate, ketoconazole, amphotericin B $\pm$ flucytosine, fluconazole

M.pachydermatis: causes fungemia in patients receiving i.v. fat emulsions; treatment: amphotericin B $\pm$ flucytosine, fluconazole

Fungi Incertae Sedis
Basal Fungal Lineages
Subphylum Entomophthoromycotina
Order Entomophthorales
Family Basidiobolaceae
Basidiobolus haptosporus: causes zygomycosis (rare); diagnosis: histology and culture of infected tissue; treatment: amphotericin B
B.ranarum: tropical regions of eastern and western Africa, southeast Asia, South America, rare cases in USA; causes painless subcutaneous nodules on lower extremities and buttocks, gastrointestinal infection, systemic infection in abnormal host (interrupted integument, neutrophil dysfunction); diagnosis: culture of clinical or surgical specimens, histopathology; treatment: surgery + itraconazole
Subphylum Mucormycotina
Order Mortierellales
Family Mortierellaceae
Mortierella: causes systemic infections in abnormal host (interrupted integument, neutrophil dysfunction)
M.hyalina: causes chronic sinusitis
Order Mucorales: pin moulds; spores borne in closed sac; uncommonly cause cellulitis (fulminant necrotising or indolent); treatment: amphotericin B
Family Cunninghamellaceae
Cunninghamella bertholletiae: causes zygomycosis; diagnosis: histology and culture of infected tissue; treatment: amphotericin B
C.elegans: causes zygomycosis (rare)—systemic infections in abnormal host (interrupted integument, neutrophil dysfunction), pneumonia in disseminated infections; diagnosis: histology and culture of infected tissue; treatment: amphotericin B
Family Mucoraceae: cause enterocolitis, infections in patients with interrupted integument, neutrophil dysfunction
Absidia: causes zygomycosis—brain and epidural abscess in neutropenics, infection in abnormal host (interrupted integument, neutrophil dysfunction), nonpyogenic meningitis (infrequent in neutropenics and impaired cell-mediated immunity), pneumonia (including diffuse interstitial), rhinocerebral mucormycosis; immunity due to phagocytes (++); diagnosis: histology and culture of infected tissue; treatment: amphotericin B
Mucor: phycomycete; dust, soil; causes mucormycosis (zygomycosis)—bagassosis and farmer's lung, brain and epidural abscess in neutropenics, adult hepatitis, nonpyogenic meningitis (infrequent in neutropenics and impaired cell-mediated immunity), pneumonia (including diffuse interstitial in granulocytopenics), localised skin lesions, 1% of fungal peritonitis in continuous ambulatory peritoneal dialysis, postseptal cellulitis in immunosuppressed, systemic infections in abnormal host (interrupted integument, neutrophil dysfunction); altered normal flora, deficiencies in neutrophils, mononuclear phagocytes, integument, ? humoral factors in infection; immunity due to phagocytes (+++); diagnosis: immunodiffusion, wet preparation, Grocott's methenamine silver stain, culture; treatment: amphotericin B, flucytosine, ketoconazole
M.amphibiorum: causes skin ulceration in platypuses
Rhizomucor pusillus: causes pneumonia (especially in leukemics)
Rhizopus: phycomycete; causes zygomycosis—brain and epidural abscess in neutropenics, infections in abnormal host (interrupted integument, neutrophil dysfunction), localised skin lesions, nonpyogenic meningitis (infrequent in impaired cell-mediated immunity), pneumonia (including diffuse interstitial); growth stimulated by excess iron; immunity due to phagocytes; diagnosis: histology and culture of infected tissue; treatment: amphotericin B
R.microsporus var rhizopodiformis: causes skin infections associated with contaminated Elastoplast bandages, systemic infections in abnormal host
Family Myocladiaceae
Myocladus corymbiferus: grows at 45°C; causes systemic infections in abnormal host
Family Saksenaeaceae
Saksenaea vasiformis: causes infection in abnormal host (interrupted integument, neutrophil dysfunction), subcutaneous zygomycosis
Phylum Microsporidia
Suborder Apansporoblastina
Family Enterocytozoonidae
Enterocytozoon bieneusi: microsporidium; causes chronic diarrhoea and malabsorption in AIDS; diagnosis: modified trichrome stain, fluorescent stain, examination of duodenal or jejunal biopsy by light or electron microscopy; treatment: albendazole
Family Nosematidae: microsporidia; cause acute diarrhoea and/or vomiting in AIDS; diagnosis: examination of stool by technique of Weber et al, Giemsa stained smear of small intestine biopsy

Nosema: microsporidium; causes enteritis in immunocompromised; report of wide distribution in body of child with *Pneumocystis* pneumonia

Family Unikaryonidae

Encephalitozoon cuniculi: microsporidium; causes chronic diarrhoea in AIDS; renal disease; sinusitis; treatment: albendazole

E.hellem: causes ocular and sinus infections

E.intestinalis: causes malabsorption and diarrhoea; diagnosis: modified trichrome stain, fluorescent stain, examination of duodenal or jejunal biopsy by light or electron microscopy; treatment: albendazole

Microsporidia Incertae Sedis

Microsporidium : causes enteritis in immunocompromised

Suborder Pansporablastina

Family Pleistophoridae

Pleistophora: microsporidium

Fungi/Metazoa Incertae Sedis

Class Ichthyosporea

Order Dermocystida

Rhinosporidium seeberi: causes rhinosporidiosis; treatment: natamycin

Stramenophiles

Phylum Bacillariophyta: diatoms

Class Bacillariophyceae: raphid, pennate diatoms

Bacillariophycidae

Bacillariales

Family Bacillariaceae

Pseudo-nitzchia pungens: causes amnesic shellfish poisoning

Blastocystis hominis: may be present in 20% or more of population; lacks a cell wall but contains mitochondria, Golgi apparatus and smooth and rough endoplasmic reticulum typical of protozoa; strictly anaerobic; pathogenicity doubtful; diagnosis: characteristic organisms in unstained, Gram stained or trichrome stained faecal smears; treatment: metronidazole, furazolidone (probably unwarranted)

Oomycetes

Order Pythiales

Family Pythiaceae

***Pythium*:** causes arteritis in thalassemic farmers; growth stimulated by excess iron; treatment: surgery + i.v. sodium iodide

Kingdom Viridiplantae

Phylum Chlorophyta

Class Trebouxiophyceae

Order Chlorellales

Family Chlorellaceae

Prototheca: achlorophyllic alga; large (8-20 μm diameter), nonbudding, spherical, ovoid or elliptical cells (theca) with prominent wall and containing several thick-walled autospores; colonies yeast-like in appearance; causes cutaneous and subcutaneous infection, olecranon bursitis, systemic infections in abnormal host; diagnosis: stains poorly in haematoxylin and eosin, stains well in Grocott's silver stain, PAS useful for observing starch grains, immunofluorescent stains, culture; treatment: surgical excision, amphotericin B $\pm$ nystatin, pentamidine, ketoconazole

P.moriformis: oval or spherical cells $>$ 9.5 μm in long dimension; capsule always present; does not assimilate trehalose, does not assimilate galactose strongly

P.stagnora: spherical cells $<$ 8.5 μm diameter; capsule common; does not assimilate trehalose, does assimilate galactose

P.wickerhamii: spherical cells $<$ 8.5 μm diameter; does assimilate trehalose, does not assimilate 1-propanol or acetate (pH 5); causes systemic protothecosis

P.zopfii: oval or spherical cells $>$ 8.5 μm diameter in long dimension; no capsule; does not assimilate trehalose, does not assimilate galactose strongly, assimilates 1-propanol and acetate (pH 5); causes systemic protothecosis

Chapter 19

Animal Parasites

Alveolata
Phylum Apicomplexa: sporozoans
Class Aconoidisada
Order Haemosporida: haemosporidians
Plasmodium: very high world prevalence; causes malaria, periodic fevers, adult hepatitis, hepatic granuloma, infections in abnormal host (infusion infection, splenic dysfunction); transmitted by bite from infected mosquito (mainly *Anopheles stephensi* in urban areas), transmitted in blood; sporozoites enter across skin epithelial surface and subsequently spread through body; carried in blood associated with erythrocytes, multiplying within them; failure to display microbial antigen on infected erythrocyte surface; polyclonal B cell activation; antigenic change; immunodepression; kidney deposits of circulating immune complexes; high overall morbidity with symptomatic clinical disease; impact on nutrition; possible clinical antagonism by malnutrition; growth stimulated by excess iron; cell-mediated immunity important in host defence (delayed hypersensitivity), also complement-fixing, neutralising, agglutinating, blocking and opsonising cytotoxic antibodies; concomitant immunity (invasion $\rightarrow$ disease $\rightarrow$ no cure $\rightarrow$ resistance to infection); diagnosis: indirect haemagglutination ($\geq$ 1:16), direct fluorescent antibody (tissue for antigen), indirect fluorescent antibody (titre $\geq$ 1:16), ELISA, thick and thin blood smears collected between chills; treatment: chloroquine, primaquine, hydroxychloroquine, amodiaquine, mepacrine, quinine, proguanil, pyrimethamine; vector control low to moderate feasibility, high priority
Subgenus *Plasmodium (Laverania)*
P.falciparum: multiple rings in erythrocytes; usually stages beyond ring forms, with exception of gametocytes, are not seen in thin smears of peripheral blood, rest of stages being thought to develop in visceral capillaries; double chromatin dots, accole forms (forms that appear on the smear to be flattened against the margin of the erythrocytes); crescent-shaped gametocytes; 8-24 merozoites; causes 22% of malaria, postneonatal pyogenic meningitis in therapy for nutritional deficiency, haemorrhagic fever; high global prevalence (44% in Chad); treatment: chloroquine, quinine, quinidine, doxycycline, tetracycline, pyrazinamide-sulphadoxine, mefloquine, halofantrine, artemisate, artemether
Subgenus *Plasmodium (Plasmodium)*
P.brasilianum: very rare human infections
P.cynomolgi: very rare human infections
P.inui: very rare human infections
P.knowlesi: very rare human infections
P.malariae: all forms of parasite in peripheral blood; band forms; 8-12 merozoites; causes 2% of malaria, quartan malarial nephropathy (relatively rare), postneonatal pyogenic meningitis (infrequent in asplenism); 44% prevalence in Chad; treatment: chloroquine
P.ovale: all forms of parasite in peripheral blood; 8-12 merozoites; enlarged erythrocytes; Schuffner's dots; fimbriated and oval erythrocytes; causes 3% of malaria
P.vivax: rare multiple rings in erythrocytes; all forms of parasite in peripheral blood; 12-24 merozoites; enlarged erythrocytes; Schuffner's dots; causes 73% of malaria; high global prevalence
P.simium: very rare human infections
Piroplasmida: piroplasmids
Family Babesiidae
Babesia: causes babesiosis in cattle and man (rare), infection in abnormal host (infusion infection, splenic dysfunction); transmitted by bite of Ixodid ticks that have fed on infected domestic or wild animals, and by blood transfusion; organism binds complement and attaches to C3b receptor on erythrocyte; carried in blood associated with erythrocytes; diagnosis: indirect haemagglutination ($\geq$ 1:32), indirect fluorescent antibody (titre $\geq$ 1:256), thick and thin blood smears; treatment: chloroquine phosphate or clindamycin + quinine or pentamidine isethionate, exchange transfusion
B.bovis: causes babesiosis in splenectomised persons (usually fatal)
B.divergens: causes babesiosis in splenectomised persons (usually fatal)
B.microti: causes babesiosis in persons with intact spleens (usually self-limited)
Family Theileriidae
Thelleria parva: tick-borne protozoal parasite causing East Coast fever (important cattle disease in East Africa); infects lymphocytes

Class Coccidia

Order Eucoccidiorida

Suborder Eimeriorina: human coccidia; complex life cycle in which both sexual and asexual reproduction may occur and intermediate hosts may or may not be used

Family Cryptosporidiidae

Cryptosporidium: coccidia that grow and reproduce within epithelial cells of respiratory and digestive organs of vertebrates; zoonosis; lacks host specificity; transmission faecal-oral (water, unpasteurised cow's milk); prevalence 0.5-3% in USA, 32% in Mexico, 50% in patients with AIDS in Haiti and Africa; incidence in Australia 1-17%; incidence highest during summer and autumn; age range 3 d to 95 years but children < 2 y greatest prevalence; causes acute diarrhoea and/or vomiting, traveller's diarrhoea, enteritis, appendicitis, cholangitis and cholecystitis; diagnosis: oocysts in fresh warm stools or duodenal aspirate (Sheather's sucrose-phenol microscopy within 2-4 minutes or immunofluorescence); treatment: discontinue immunosuppressive drugs, spiramycin, erythromycin, paromomycin, immune bovine dialyzable leucocyte extract

C.felis: human pathogen

C.hominis: primarily infects humans, but infections in dugong, lamb, cattle reported

C.meleagridis: human pathogen

C.muris: possible human pathogen

C.parvum: affects rodents, calves, lambs and other mammals as well as humans; causes cryptosporidosis (self-limiting gastroenteritis (watery diarrhoea and fever) in persons with immune response, chronic diarrhoea, potentially fatal, in those with impaired immune response (T helper lymphocyte dysfunction); attack rate 50-66% in day care centres, 14% in family members); transmitted in water (source animal and human feces); cause of largest water-borne outbreak in history (Milwaukee, 1993): 400,000 affected, with 85 deaths; interferon-γ active in experimental infections

Family Eimeriidae: coccidia in which entire growth period (asexual and sexual through development of unsporulated oocyst) is passed within host cell

Cyclospora cayetanesis: infections reported from Americas, Africa, Indian subcontinent, South-East Asia, New Guinea; acquired from water and contaminated food (basil, lettuce, raspberries); causes enteritis; diagnosis: unsporulated oocysts in wet film or modified acid-fast stain; treatment: cotrimoxazole

Eimeria: causes coccidiosis in domestic animals (may cause diarrhoea and blood loss); attaches to and penetrates epithelium of large intestine, causing disease by killing epithelial cells and inducing diarrhoea; found in stools in man but believed ingested and passed as unaltered oocysts; no real evidence of pathogenicity in man

Isospora: causes isosporiasis (coccidial colitis, coccidial diarrhoea, coccidial dysentery, intestinal coccidiosis, isoporosis); usually acquired through ingestion of mature (viable) oocysts, eg. in contaminated food or drink; oocysts produce 2 sporoblasts mating into 2 sporocysts, each of which develops 4 sporozoites

Family Sarcocystidae

Cystoisospora belli: cosmopolitan but uncommon (0.2% of patients with AIDS in USA, 15% of patients with AIDS in Haiti); causes acute diarrhoea and/or vomiting in AIDS, enteritis, infections in T helper lymphocyte dysfunction; diagnosis: finding immature or mature oocysts in fresh stool or concentrate (multiple examinations may be required), Charcot-Leyden crystals common; treatment: cotrimoxazole

Sarcocystis: cosmopolitan but rare; wide range of hosts including humans; obligatory 2 host (predator-prey) life cycle; causes sarcocystosis (*Sarcocystis*-induced coccidiosis, sarcosporidiosis)—intestinal sarcocystosis caused by number of species for which dogs, cattle and other animals serve as intermediate hosts and diagnosed by finding mature oocysts containing sporocysts and/or free sporocysts each containing 4 sporozoites in fresh stool or concentrate, and muscle sarcosporidiosis in which humans are dead-end intermediate host for many species and infection is detected by histologic demonstration of cysts in muscle tissue; acquired by ingestion of raw or partly cooked meat containing cysts

Sarcocystis hominis: found in 0.3% of homosexual men; causes enteritis; local irritation and damage and nutrient malabsorption

S.suihominis: causes sarcocystosis

Toxoplasma: causes toxoplasmosis, adult hepatitis, hepatic granuloma, pneumonia, erythema nodosum, systemic infections in cell-mediated immunity disorders; multiplies in macrophages; growth stimulated by excess iron; ? antigenic change, immunodepression, polyclonal activation; immunity due to delayed type hypersensitivity, complement-fixing, neutralising, agglutinating and opsonising cytotoxic antibodies, ? blocking antibodies; treatment: sulphadiazine + pyrimethamine, cotrimoxazole

T.gondii: causes toxoplasmosis, anterior uveitis, brain abscess in impaired cell-mediated immunity, encephalitis (3-40% of AIDS patients), adult hepatitis, hydrocephalus, lymph gland infection (localised or general), nonpyogenic meningitis in immunosuppressed, mental retardation, diffuse interstitial pneumonia, pancreatitis (7% of cases in AIDS), stillbirth, prenatal meningitis, retinochoroiditis, infection in abnormal host (infusion infection, T helper lymphocyte dysfunction); widely distributed in animals and birds; transmitted by blood transfusion or transplacental infection of foetus during initial infection of mother (tachyzoite), ingestion of cyst (spherical, 100-200 μm diameter; dormant form, resistant to chemotherapeutic

agents, drying, gastric acid) in uncooked, undercooked or unfrozen meat, or of oocysts (spherical, 10-12 μm diameter; shed in faeces of members of cat family after cysts ingested in raw meat; highly resistant to desiccation in cat faeces), subsequently spreads through body; cysts and tachyzoites (crescentic, 2-4X4-8 μm; rapidly proliferating form that causes tissue injury and disease; susceptible to chemotherapy) intracellular in eye, tachyzoites intracellular in spleen; inhibits attachment to polymorph, lysosome-phagosome fusion and degranulation; carried in blood associated with mononuclear cells; persists in lymphoid tissue, muscle (cysts and tachyzoites intracellular in cardiac and skeletal muscle) and brain (cysts and tachyzoites in cells and interstitial fluid; may be infectious, not shed to exterior), activation causing neurological disease; immunity cell-mediated (delayed type hypersensitivity-activated macrophage +++); susceptible to interferon-γ and interferon-β-stimulated macrophages; interleukin-2, interleukin-12 and tissue necrosis factor also induce antimicrobial activity; diagnosis: indirect haemagglutination (≥ 1:1024), direct fluorescent antibody (tissue for antigen), indirect fluorescent antibody (titre ≥ 1:1024 = recent infection; IgM = recent or congenital infection), immunodiffusion, complement fixation test (≥ 1:8), ELISA, Sabin-Feldman dye test (≥ 1:1024), latex agglutination, IgG avidity, mouse inoculation; treatment: sulphadiazine or trisulphapyrimidine + pyrimethamine, cotrimoxazole, spiramycin, 5-fluorouracil, clindamycin

Ciliophora

Subphylum Intramacronucleata

Class Litostomatea

Subclass Trichostomatea

Order Vestibuliferida

Family Balantidiidae

Balantidium: more or less ovoid shape, conspicuous cytostome, ciliated covering over entire body, contractile vacuoles, conspicuous, slightly curved macronucleus and minute micronucleus

B.coli: ciliate; common parasite of large intestine of pig; rare in humans but wide distribution in temperate and warm climates and endemic among pig farmers in Papua New Guinea; causes balantidiasis (80-85% asymptomatic; dysentery, enteritis, peritonitis (very rare), vaginitis (very rare), appendicitis (exceedingly rare)); infection of man from pigs by ingestion of cysts; trophozoites in ulcers and free in lumen of large intestine; diagnosis: demonstration by direct microscopic examination of trophozoites (size and characteristic morphology) in more diarrhoeic stool or scraping of colonic mucosa or cysts (may be intermittent) in formed stool; treatment: metronidazole, tetracycline, paromomycin, diodohydroxyquine, chloroquine, resection of affected portions of gastrointestinal tract in invasive infections

Dinophyceae: appear to be a bridge between prokaryotes and eukaryotes; most with 2 flagella; most marine; some produce powerful respiratory toxins; create 'red tides'

Order Dinophysiales

Family Dinophysiaceae

Dinophysis: causes diarrhoeal shellfish poisoning

Order Gonyaulacales

Family Goniodomaceae

Gambierdiscus toxicus: 'indigenous' to sea water; causes ciguatera fish poisoning; treatment: supportive, i.v. mannitol, tocanide, amitryptyline, nifedipine

Family Gonyaulacaceae

Alexandrium: 'indigenous' to ballast and sea water; causes paralytic shellfish poisoning

Gonyaulax : causes paralytic shellfish poisoning; treatment: supportive

Order Gymnodiniales

Family Gymnodiniaceae

Karenia brevis: dinoglagellate; 'indigenous' to ballast and sea water; causes neurotoxic shellfish poisoning; treatment: supportive

Order Peridiniales

Family Pfiesteriaceae

Pfiesteria piscicida: responsible for killing enormous numbers of fish in Chesapeake Bay on US Atlantic seacoast, and for memory loss and skin problems in fishermen

Amoebozoa

Archamoebae

Entamoebidae

Endolimax: parasitic amoeba of small size, having a vesicular nucleus; generally 1 nucleus in trophozoite, with a comparatively large, irregular, eccentric karyosome attached by several achromatic threads to a delicate nuclear membrane; no peripheral chromatin granules; forms cysts

E.nana: trophozoite 6-12 μm (usual range 8-10 μm), sluggish, usually nonprogressive, with blunt pseudopodia, 1 nucleus, occasionally visible in unstained preparations, no peripheral chromatin, karyosomal chromatin large, irregularly shaped, blotlike, cytoplasm granular, vacuolated, contains bacteria; ripe cyst 5-10 μm (usual range 6-8 μm), spherical, ovoid or

ellipsoidal, with 4 nuclei, immature cysts with < 4 rare, no peripheral chromatin, karyosomoal chromatin large, blotlike, usually central, occasionally chromatid granules or small oval masses, glycogen rarely present, usually diffuse, concentrated mass occasionally in young cysts, stains reddish-brown with iodine, chromatoids absent; frequently inhabits lumen of large intestine; cosmopolitan (14% of travellers from tropics, 16% of homosexual men, 4% in male Haitian entrants to USA); nonpathogenic; diagnosis: demonstration of trophozoites or cysts in faeces

Entamoeba: endoparasitic amoebae which have a more or less distinct nucleus (generally 1 nucleus in trophozoite), a relatively small spherical karyosome at or near centre of nucleus, peripheral layer of fine chromatin beads or granules lining distinct nuclear membrane; human-human transmission by ingestion of cysts; growth stimulated by excess iron

E.coli: trophozoites 15-50 μm (usual range 20-25 μm), motility sluggish, nonprogressive, with blunt pseudopods, 1 nucleus, often visible in unstained preparations, peripheral chromatin coarse granules, irregular in size and distribution, karyosomal chromatin large, discrete, usually eccentrically located, cytoplasm coarse, often vacuolated, contains bacteria; ripe cyst 10-35 μm (usual range 15-25 μm), usually spherical, occasionally oval, triangular or another shape, with 8 nuclei, occasionally supernucleate cysts with 16 or more, immature cysts with 2 or more occasionally, peripheral chromatin present, coarse granules irregular in size and distribution but appear more uniform than in trophozoites, karyosomal chromatin large, discrete, usually eccentric but occasionally central, glycogen in early stages only, large chromatids occasionally present but often absent, usually splinterlike with pointed ends; prevalence +++ (12% of travellers from tropics, 14% of homosexual men, 5% of Haitian entrants to USA); commensal (colonisation → no disease) lumen parasite of large bowel; viable cysts passed in faeces transmitted to new host by contaminated food or drink or by fingers or fomites contaminated with faeces; diagnosis: demonstration of trophozoites or cysts in faeces

E.dispar: morphologically identical to *E.histolytica* but does not cause invasive disease

E.gingivalis: normal flora of mouth; found in gingival tissues; more common in the presence of inflammation

E.hartmanni: trophozoites 5-12 μm (usual range 8-10μm), usually nonprogressive motility but may be progressive occasionally, 1 nucleus, not visible in unstained preparations, peripheral chromatin similar to *E.histolytica*, karyosomal chromatin small, discrete, often eccentrically located, cytoplasm finely granular, contains bacteria; cysts 5-10 μm (usual range 6-8 μm), usually spherical, 4 nuclei in mature cyst, immature cysts with 1 or 2 often seen, chromatin similar to *E.histolytica*, chromatid bodies present, elongated bars with bluntly rounded ends, glycogen similar to *E.histolytica*; prevalence + (0.3% of travellers from tropics, 2% of homosexual men, 1% of Haitian entrants to USA); commensal in lumen of large intestine; diagnosis: demonstration of trophozoites or cysts in faeces

E.histolytica: trophozoites 10-60 μm (usual range > 20 μm), motility progressive with hyaline, fingerlike pseudopods, 1 nucleus, not visible in unstained preparations, peripheral chromatin fine granules, usually evenly distributed and uniform in size, karyosomal chromatin small, discrete, usually central but occasionally eccentric, cytoplasm finely granular, may contain erythrocytes; ripe cysts 10-20 μm (usual range 12-15 μm), usually spherical, with 4 nuclei, immature cysts with 1 or 2 occasionally, peripheral chromatin present, fine uniform granules, evenly distributed, karyosomal chromatin small, discrete, usually central, glycogen diffuse, concentrated mass often present in young cysts, stains reddish-brown with iodine, large chromatids generally present, elongated bars with bluntly rounded ends; prevalence high; global mortality 75 000/y (74 000 in developing world); case-fatality rate up to 47%; impact on nutrition with symptomatic clinical disease; causes amoebiasis (amebiasis, amoebosis, entamoebiasis), brain abscess, colitis, acute diarrhoea and/or vomiting, amoebic dysentery (1% of infective diarrhoea in adults), appendicitis, adult hepatitis, hepatic 'abscess' (bacteriologically sterile necrotic foci filled with proteinaceous debris rather than pus; most frequent in adult males), hepatic granuloma, pulmonary abscess, traveller's diarrhoea, urethritis in homosexual males, cutaneous amoebiasis; transmission by ingestion of cysts; attaches to and penetrates epithelium of large intestine, causing disease by killing epithelial cells and inducing diarrhoea by mucosal damage and inflammation; rarely invades subepithelial tissues and subsequently spreads through body (especially to liver); trophozoites in brain parenchyma, in tissue of genitourinary system (vagina, cervix, penis), in ulcers in large intestine, in liver and lung parenchyma, in wall of skin ulcer; cysts free in lumen of large intestine; shows leucotoxicity; diagnosis: combination of MIF staining and formalin-ethyl acetate concentration, direct smear of fresh stool to observe amoeboid motility, iron-haematoxylin or trichrome stain, serology (commonly available—indirect haemagglutination and counterimmunoelectrophoresis (most sensitive and specific), latex agglutination, immunodiffusion (agar gel diffusion), ELISA; evaluated—bentonite flocculation, indirect immunofluorescence, immunoelectrophoresis); treatment: metronidazole, tinidazole, emetine, dihydroemetine, chloroquine, iodoquinol, diloxanide furoate, paromomycin, iodoquinol; prevention and control by water and sanitation moderately feasible, moderate priority; health education, adequate diagnosis and correct treatment of invasive amoebiasis, implementation of surveillance and control programs also important

E.polecki: trophozoites 10-25 μm (usual range 15-20 μm), usually sluggish motility, occasionally progressive in diarrhoeic specimens, 1 nucleus, may be slightly visible in unstained preparations, occasionally distorted by pressure from vacuoles in cytoplasm, peripheral chromatin usually fine granules evenly distributed, occasionally irregularly arranged, sometimes in plaques or crescents, karyosomal chromatin small, discrete, eccentric, occasionally large, diffuse or irregular, cytoplasm granular, with numerous vacuoles, contains bacteria and yeasts; cysts 9-18 μm (usual range 11-15 μm), spherical or oval, 1 (rarely 2) nucleus, occasionally visible in unstained preparations, peripheral chromatin usually fine granules evenly

distributed, karyosomal chromatin usually small and eccentric, chromatoid bodies present, many small bodies with angular or pointed ends or few large ones, may be oval, rodlike or irregular, glycogen usually small, diffuse masses, stains reddish-brown with iodine, dark inclusion mass often present, does not stain with iodine; usually considered rare but multiple cases found in SE Asian refugees; probably widely distributed; primarily parasite of hogs and monkeys; usually considered nonpathogenic but found in patients with loose stools or diarrhoea; diagnosis: demonstration of trophozoites or cysts in faeces; treatment: diloxanide furoate 500 mg three times daily for 10 d

'Iodamoeba': generally 1 nucleus in trophozoite; large, central, spherical karyosome rich in chromatin, surrounded by layers of achromatic granules or globules and anchored to the nuclear membrane by achromatic filaments; in endoplasm, 1, or at times 2, well-circumscribed glycogen vacuole, invariably present in cyst, occasionally seen in trophozoite; no peripheral chromatin

'I.bütschlii': trophozoites 8-20 μm (usual range 12-15 μm), motility sluggish, usually nonprogressive, 1 nucleus, usually not visible in unstained preparations, no peripheral chromatin, karyosomal chromatin large, usually central, surrounded by refractile, achromatic granules (often not distinct), cytoplasm coarse, granular, vacuolated, contains bacteria, yeasts, other material; ripe cysts 5-20 μm (usual range 10-12 μm), ovoid, ellipsoidal, triangular or other shape, with 1 nucleus, no peripheral chromatin, karyosomal chromatin large, usually eccentric, refractile, achromatic granules on one side of karyosome (indistinct in iodine preparations), glycogen in a dense mass, stains dark brown with iodine, no chromatoids; inhabits lumen of large intestine; cosmopolitan (2% of male Haitian entrants to USA, 3% of travellers from tropics, 13% of homosexual men); no evidence of pathogenicity for man; diagnosis: demonstration of trophozoites or cysts in faeces

Diplomonadida Group

Diplomonadida

Family Enteromonadidae: 3 anterior flagella and a fourth trailing flagellum, lack axostyle and other axial organelles

Enteromonas hominis: fairly frequently found in large intestine and stool specimens, especially from patients with diarrhoea, but unlikely to be pathogenic; probably enters body through ingestion of viable cysts in contaminated food or drink; diagnosis: unstained trophozoites anterior flagella, trailing flagellum, no undulating membrane, stained trophozoites absence of a costa, axostyle or cytostomal fibrils, single nucleus with large anterior karyosome, small size, stained cysts oval shape, 1-4 nuclei with preponderance of binucleate forms, small size

Family Hexamitidae: 2 nuclei lying side by side in transverse plane; 6-8 flagella in 3 or 4 pairs; in some genera, paired axonemes; generally show bilateral symmetry

Subfamily Giardinae

Giardia: trophozoites rounded anteriorly and tapered posteriorly, have convex dorsal surface and flattened ventral side with a shallow sucking disc in its anterior portion and 4 pairs of flagella arising from a complicated system of axonemes; cysts are ovoid to ellipsoidal and have thin, tough wall from which cytoplasm is characteristically separated

G.lamblia: flagellate; high global prevalence (cosmopolitan; worldwide 200 M; most frequently identified organism in stools; 2-15% of immigrants, 27% of immigrant children, 19% of Guatemalan children, 6% of SE Asian refugees, 5% of travellers from tropics, 2% of homosexual men, 7% in USA, 3% in temperate climates (up to 20% in children), 25% in tropical areas; half of all instances of diarrhoea in primary hypogammaglobulinemia); causes giardiasis (giardosis, lambliasis, lamblosis; low grade intestinal disease of upper small intestine and gall bladder; most frequently asymptomatic but acute or chronic disease—acute diarrhoea (incubation period 15 d; lasts > 5 d; recurrent and mucoid; 1% of infective diarrhoea in adults; up to 2% of traveller's diarrhoea) and/or vomiting, nursery infection, chronic diarrhoea and failure to thrive in children in tropical areas, chronic intestinal malabsorption—may result; predisposing factors blood group A, primary hypogammaglobulinema, protein-energy malnutrition (in association with hypochlorhydria and pancreatitis), in children in developing countries, 25% of waterborne disease outbreaks (derived from animal and human faeces), infection in abnormal host (γ-globulin dysfunction); faecal-oral transmission (human-human) by ingestion of viable cysts in contaminated food or drink; oral infectious dose in man 10-100 cysts; also direct transmission in day care centres and between sexual partners in homosexual males; attack rate 17-90% in day care centres, 12-50% in family members; incubation period 12-19 d; attaches to intestinal epithelium by mechanical sucker; replicates attached to intestinal epithelium; infection generally confined to epithelial surface of intestinal tract; diarrhoea not always produced, mechanism not understood; probable impact on nutrition (achlorhydria/hypochlorhydria, impaired protein digestion, bacterial overgrowth, local irritation and damage to microvilli underlying trophozoites, malabsorption of D-xylose and vitamin B_{12} in 55-60%, steatorrhoea in 25-50%); recovery from primary infection due to antibody (interference with adherence +++), cell-mediated (+); diagnosis: demonstration of trophozoites in diarrhoeic, and cysts in formed, stools by modified Ritchie formalin-ether concentration, demonstration of trophozoites in duodenal or jejunal aspirate or by use of duodenal 'capsule'; counterimmunoelectrophoresis reported as sensitive and reliable in combined examination of faeces and duodenal fluid, ELISA (92% sensitivity, 98% specificity) reported; treatment: metronidazole (> 99% cure rate with 15 mg/kg/d to 250 mg 3 times a day for 5-10 d), quinacrine, furazolidone, tinidazole, albendazole, paromomycin; prevention and control by intermittent treatment of those infected, improved water supply and sanitation, education high feasibility and priority

Family Retortamonadidae: 2 flagella, 1 of which is directed anteriorly, a second posteriorly and trailing, both arising from a blepharoplast immediately in front of an anteriorly situated nucleus

Chilomastix: trophozoites rounded anteriorly and attenuated posteriorly, 3 anteriorly directed free flagella and a more delicate one within a prominent cytostome; cysts pear or lemon shaped, with rather thick wall, show clearly a large cytostome

Chilomastix mesnili: cosmopolitan; frequently found in caecal region of large intestine and in stools (2% of travellers from tropics, 0.9% of homosexual men); unlikely to be pathogenic; normally no signs or symptoms but some authors have reported diarrhoea associated with very large numbers of organisms (chilomastixiosis, chilomastixiasis, chilomastosis); infection from ingestion of viable cysts in contaminated food or drink; diagnosis: unstained trophozoites anterior flagellum and spiral groove, stained trophozoites single anterior nucleus, cyclostome with a curved, shepherd's crook fibril, no costa or undulating membrane, unstained cysts protuberance at one end of lemon-shaped cyst, stained cysts single, large nucleus and curved cytostomal fibril

Retortamonas: relatively plastic body which is pyriform, ovoid or fusiform and is attenuated posteriorly; rare; probably non-pathogenic

Centramoebida

Acanthamoebida

Acanthamoeba: causes acanthamoebiasis (granulomatous amoebic meningoencephalitis; insidious neurologic changes in debilitated or immunosuppressed patients who usually have no history of recent exposure to fresh water; CNS infection secondary to some other focus; death after a more chronic course), nonpurulent conjunctivitis, keratitis and iritis, anterior uveitis, pneumonitis, sinusitis and disseminated infection in AIDS; diagnostic stage in CNS and eye; treatment: amphotericin B + miconazole + rifampicin, propanidine isethionate, bibromopropanidine isethionate, clotrimazole + neomycin or gentamicin

A.astronyxis: isolated from human CNS

A.castellani: isolated from human CNS, eye (keratitis and iritis)

A.comandoni: not isolated from human infections

A.culbertsoni: isolated from human CNS, eye (keratitis and iritis)

A.griffini: not isolated from human infections

A.hatchetti: isolated from human eye (keratitis and iritis)

A.lenticulata: not isolated from human infections

A.palestinensis: isolated from human CNS

A.polyphaga: isolated from human CNS, eye (keratitis and iritis)

A.rhysoides: isolated from human CNS, eye (keratitis and iritis)

A.royreba: not isolated from human infections

A.tubiashi: not isolated from human infections

Euglenozoa

Order Kinetoplastida: kinetoplasts

Family Trypanosomatidae

Leishmania: flagellate; causes leishmaniasis (leishmaniosis), adult hepatitis, kala azar, oriental sore, infections in T helper lymphocyte dysfunction; reservoir in canines such as wild dogs, foxes, genets and hyrax, additionally on occasion in rats; transmission from animal host to man via sandflies (*Phlebotomus)* by inoculation of promastigotes, and from man to man by direct contact; multiplies in macrophages; carried in blood associated with mononuclear cells; antigenic depletion by capping and shedding of surface antigens; polyclonal activation ±; growth stimulated by excess iron; primary immune defence activation of phagocytes, by T cell-generated lymphokines, rendering them resistant to infection; killing of infected phagocyte (delayed hypersensitivity), complement-fixing, neutralising, agglutinating and opsonising cytotoxic antibodies also important; diagnostic stage in skin; treatment: chloroquine, hydroxychloroquine, amodiaquine, mepacrine, quinine, primaquine, proguanil, pyrimethamine

L.aethiopica

***L.donovani* species complex:** *L.chagasi, L.donovani, L. nfantum* and possibly other undescribed species; India, Mediterranean, E Africa, Middle East, S Africa, China, Latin America; high global prevalence; cause cutaneous (rare) and visceral leishmaniasis; sandfly vector; human, dog, fox, rodent, jackal reservoirs; intracellular survival within macrophages by resistance to microbicidal events; susceptible to granulocyte-macrophage colony stimulatory factor-stimulated macrophages; interleukin-1 and interleukin-2 also induce antimicrobial activity; interferon-γ and tissue necrosis factor also active in experimental infections; diagnosis: examination of bone marrow smears, splenic pulp smears, liver biopsy, thin smears of buffy coat of blood, lymph node aspirate or biopsy, culture of tissue or blood, ELISA, indirect haemagglutination test, direct agglutination titre, complement fixation test, latex agglutination, Montenegro skin test; treatment: sodium stibogluconate, γ-interferon, allopurinol, pentamidine isethionate, metronidazole

L.major

***L.mexicana* complex:** *L.amazonensis, L.enrettii, L. mexicana, L.pifanoi*; high global prevalence; cause New World cutaneous leishmaniasis, nasopharyngeal and oronasal leishmaniasis (rare); resists lysosomal enzymes; treatment: sodium stibogluconate, amphotericin B, metronidazole, ketoconazole, pentamidine isethionate, allopurinol, interleukin 2

***L.tropica*:** high global prevalence; cause Old World cutaneous leishmaniasis, visceral leishmaniasis (rare); sterilising immunity (invasion → disease → cure); susceptible to tissue necrosis factor-stimulated macrophages; treatment: sodium stibogluconate, paromomycin, methylbenzethonium

Subgenus *Viannia*

***L.braziliensis* species complex:** *L.braziliensis, L.columbiensis, L.equatorensis, L. peruviana*; high global prevalence; cause New World cutaneous and mucocutaneous leishmaniases; treatment: sodium stibogluconate, amphotericin B, metronidazole, ketoconazole, pentamidine isethionate, allopurinol, interleukin 2

L.braziliensis: causes espundia

L.garnhami

***L.guayanensis* species group**

L.guayanensis

L.panamensis

Trypanosoma: flagellate; transmission by biting insects (African: tse tse fly; American: reduviid); animal reservoir; 2 species pathogenic for man, causing trypanosomiasis; metacyclic trypomastigotes enter across skin epithelial surface and subsequently spread through body; multiplies within macrophages (American, some African) and outside cells (African); carried in blood free in plasma; growth stimulated by excess iron; microbial antigens vary within individual host (sequential adoptive phenotypic variation); causes immunodepression and polyclonal activation; primary immune defence activation of phagocytes by T cell-generated lymphokines, rendering them resistant to infection, and killing of microbe extracellularly by complement-mediated lysis or intracellularly by opsonised phagocytosis and killing; killing of infected phagocyte and neutralisation of microbial toxins also important; diagnostic stage in plasma, gastrointestinal tract, lymph node, muscle, heart; diagnosis: thick and thin blood films and buffy coat examination (febrile stage)

Subgenus *Herpetosoma*

Trypanosoma rangeli: found in human blood but causes no specific signs or symptoms and is not believed to be pathogenic for man; believed to be transmitted by bite of insects of genus *Rhodinus*

Subgenus *Schizotrypanum*

Trypanosoma cruzi: high global prevalence; causes American trypanosomiasis (Chaga's disease), achalasia, infusion infections; transmitted by Reduviidae; transmitted in blood; persists in blood (trypomastigote free in blood) and macrophage (intracellular survival due to escape from lysosomes; may be infectious, not shed to exterior), causing chronic disease; amastigote in neuroglia cells in brain, in Kupfer cells in liver, intracellular in lymph nodes and cardiac muscle and in reticuloendothelial cells of spleen; ineffective immunity (invasion → disease response → no resistance or cure); ? antigenic mimicry by coating of parasite by immunoglobulin fractions (fabulation); diagnosis: Machado-Geurrein test, indirect fluorescent antibody titre, haemagglutination inhibition test, culture of blood and bone marrow aspirate on biphasic blood agar medium, xenodiagnosis; treatment: nifurtimox

Subgenus *Trypanozoon*

Trypanosoma brucei brucei: causes African trypanosomiasis, sleeping sickness; natural resistance (no invasion); transmitted in blood; diagnosis: Giemsa stained smears of fluid aspirated from enlarged lymph gland, bone marrow aspirate, CSF, ELISA; treatment: suramin, melarsopol, nitrofurazone, difluoromethylornithine hydrochloride monohydrate

T.brucei gambiense: high global prevalence; causes West African trypanosomiasis; transmitted by *Glossina palpalis, Glossina fusiceps* and *Glossina tachinoides*; trypomastigote free in blood, in parenchyma and blood in brain, in fluid in lymph nodes; treatment: as for *Trypanosoma brucei* + pentamidine isethionate

T.brucei rhodesiese: high global prevalence; causes East African trypanosomiasis, haemorrhagic fever; transmitted by *Glossina morsitans, Glossina pallidipes, Glossina sywnnertoni* and (around Lake Victoria) *Glossina fusiceps*; trypomastigote free in blood, in parenchyma and blood in brain, in fluid in lymph nodes; treatment: as for *Trypanosoma brucei*

Kingdom Metazoa

Eumetazoa

Bilateria

Acoelomata

Phylum Platyhelminthes: flat worms; flattened, segmented or unsegmented; gut may or may not be present; no body cavity, viscera in gelatinous matrix

Cestoda: tapeworms; segmented; possess scolex, neck and proglottids; hermaphroditic; reproduction oviparous, sometimes multiplication within larval forms; infection generally by encysted larvae; cause cestodiasis

Subclass Eucestoda
Order Cyclophyllidea
Family Davaineidae
Raillietina: common parasites of chicken, pigeon and other birds
Family Dipylidiidae
Dipylidium caninum: dog tapeworm; common parasite of dogs and cats; of minor importance in human infections (causes dipylidiasis (dog tapeworm infection), mainly in children, acquired by ingestion of infected fleas); adults free in lumen of small intestine (scolex attached)
Family Hymenolepididdidae
Hymenolepis: causes hymenolepiasis (hymenolepidosis; disease only results from heavy infection; mild infection usually asymptomatic); diagnosis: ova in faeces 30 d after infection; treatment: praziquantel, niclosamide, paromomycin
H.diminuta: rat tapeworm; ova spherical, 80-98 μm, striated shell, yellow, polar filaments absent; of minor importance in human infections (hymenolepiasis due to *H.diminuta* (hymenolepiasis diminuta, rat tapeworm infection) is uncommon, clinically resembles that due to *H.nana*, and is acquired by ingestion of infected fleas or beetles)
H.nana: dwarf tapeworm; ova oval or spherical, 48-55X55-62 μm, shell nonstriated, colourless, polar filaments present; present in 0.1% of travellers from tropics; hymenolepiasis due to *H.nana* (dwarf tapeworm infection, hymenolepiasis nana) is a result of heavy intestinal infection; infection is acquired by ingestion of ova or (in autoinfection) cysticercoids
Family Mesocestoididae
Mesocestoides lineatus: recovered from man on rare occasions in Japan but pathogenicity uncertain
Family Taeniidae
Echinococcus: tapeworm of animals; larval stage causes echinococcosis, adult hepatitis, thyroiditis; 1 of most important helminthiases transmitted from animals to man; diagnostic stage in CNS, liver, spleen, lung; diagnosis: eosinophilia, identification of scolices, larval capsules or daughter cysts, complement fixation test, indirect haemagglutination titre, counterimmunoelectrophoresis, RAST, bentonite flocculation test, latex agglutination, indirect immunofluorescene, immunodiffusion, passive haemagglutination; treatment: thiabendazole, albendazole
E.granulosus: hydatid worm; causes echinococcosis (cystic echinococcosis, *Echinococcus* disease, unilocular echinococcosis, unilocular hydatid disease, unilocular hydatidosis; chronic disease, usually of liver or lungs, less frequently brain, bone or other organs; larvae become lodged in an organ and produce a well-defined, usually spherical, hydatid cyst, which may rupture and cause anaphylactic or allergic reactions and dissemination to other organs; acquired by ingestion of ova spread by infected dogs), enteritis, raised intracranial pressure; diagnosis: X-ray, serology; treatment: surgery
E.multilocularis: alveolar hydatid worm; causes echinococcosis (alveolar echinococcosis, alveolar hydatid, alveolar hydatid cyst, alveolar hydatid disease, alveolar hydatidosis, malignant hydatid, multilocular echinococcosis, multilocular hydatidosis; larvae produce tumour-like alveolar cysts that spread by direct tissue infiltration (as a rule, small vesicle develops initially and soon, through both exogenous and endogenous budding of germinative membrane, new small cysts are given off in every direction until they finally form a tight cluster of small vesicles); liver most frequently invaded organ; less common than echinococcosis due to *E.granulosus*; usually fatal if not treated; usually acquired by accidental ingestion of ova from excreta of infected foxes, dogs or cats), enteritis
E.oligarthus: causes echinococcosis (polycystic hydatid disease; most commonly in liver but cysts may spread to other sites; uncommon; acquired by accidental ingestion of ova from faeces of infected dogs)
E.vogeli: uncommon cause of echinococcosis (polycystic hydatid disease; Central America and Northern S America; acquired by accidental ingestion of ova from faeces of infected dogs
Taenia: present in 1% of El Salvadorean refugees, 130 M infected worldwide; causes taeniasis; cysticerci enter orally; treatment: niclosamide, praziquantel, paromomycin
T.crassiceps: 1 report of disease similar to cysticercosis
T.multiceps: 'gidworm'; larval forms cause coenurosis (coenuriasis) in herbivorous animals, especially sheep (gid, staggers, sturdy) and, rarely, in man (cerebral or ocular (cysts usually beneath conjunctiva)); acquired by accidental ingestion of eggs
T.saginata: beef tapeworm; prevalence in humans from 0.02% in USA to 30% in some areas of W Africa; 0.1% in travellers from tropics; prevalence in cattle from 0.06% in USA to 10% in E Africa; common cause of taeniasis (beef tapeworm infection, taeniasis saginata; enteritis, appendicitis, cholangitis and cholecystitis); adults free in lumen of small intestine (scolex attached); transmission vertebrate-human by ingestion of cysticerci; diagnosis: gravid segments, ova, scolices in faeces; treatment: praziquantel, thiabendazole
T.serialis: larval forms produce cysts in man
T.solium: pork tapeworm; causes cysticercosis (cysticercal disease, cysticerciasis, cysticercus disease, *Taenia solium* cysticercosis; disease caused by larval form), enteritis (pork tapeworm infection, taeniasis solium; infection of intestine with adult tapeworm), eye infections, nonpyogenic meningitis (infrequent in impaired cell-mediated immunity), thyroiditis; cysticerci in brain parenchyma, in vitreous and anterior chamber of eye, in subcutaneous tissue and in skeletal and cardiac muscle; adults free in lumen of small intestine (scolex attached); transmission vertebrate-human by ingestion of embryonated

eggs in contaminated food or water (source animal and human faeces), or autoinfection by ingestion of cysticerci; diagnosis: segments, ova, scolices in faeces or from perianal area, haemagglutination of serum and CSF, ELISA, enzyme-linked immunoelectrotransfer blot assay, indirect fluorescent antibody titre, histology of biopsied nodules; treatment: mebendazole, albendazole, praziquantel (+ dexamethasone or prednisone in neurocysticercosis)

T.taeniaeformis: less frequent cause of taeniasis

Order Pseudophyllidea

Family Diphyllobothriidae

Digramma: twice found in man; believed to cause anaemia

Diphyllobothrium: causes diphyllobothriasis (bothriocephaliasis, bothriocephalosis, broad tapeworm infection, dibothriocephaliasis, *Dibothriocephalus* anemia, fish tapeworm infection, tapeworm anaemia; common intestinal infection (enteritis) acquired from eating raw or inadequately cooked fresh-water fish); diagnosis: ova or proglottids in faeces or vomitus; treatment: niclosamide, praziquantel, paromomycin

D.cordatum: occasional cause of diphyllobothriasis

D.latum: fish tapeworm of man; most frequent cause of diphyllobothriasis (enteritis, achlorhydria/hypochlorhydria, competition for nutrients); cysticerci enter orally; adults free in lumen of small intestine (scolex attached)

D.pacificum: occasional cause of diphyllobothriasis

Diplogonoporus grandis: tapeworm occasionally found in man, producing disease manifested by abdominal pain, alternating diarrhoea and constipation, and anemia

Ligula intestinalis: found in man on rare occasions

Spirometra: causes spirometrosis (larval diphyllobothriasis, *Sparganum* infection, sparganosis; larvae migrate through subcutaneous tissue; almost any tissue may be invaded, including brain, breast, joints, muscle, spermatic cord); treatment: thiabendazole

S.erinaceieuropaei: causes spirometrosis

S.mansonoides: causes spirometrosis

Trematoda: flukes; unsegmented; leaf-like or cylindrical; generally hermaphroditic; digenetic reproduction oviparous or multiplication within larval forms; infection mainly by larval stages entering intestinal tract, sometimes through skin; cause trematodiasis

Subclass Digenea: flukes

Order Azygiida

Family Isoparorchiidae

Isoparorchis hypselobagri: found in human intestine on very rare occasions

Order Echinostomida

Suborder Echinostomata

Superfamily Echinostomatoidea

Family Cathaemasiidae

Cathaemasia: parasite of birds; 1 case of disease (epigastric pain and soft stools) reported from Philippines; infection attributed to eating raw snails

Family Echinostomatidae

Echinoparyphium: parasite of birds found once in man but pathogenicity uncertain

Echinostoma: causes echinostomiasis (Garrison's fluke infection); acquired by eating raw or inadequately cooked infected molluscs (second intermediate host); usually asymptomatic but intestinal colic and diarrhoea in heavy infection

E.revolutum: causes echinostomiasis

Himasthla: found in man but pathogenicity uncertain

Family Fasciolidae

Fasciola: causes fascioliasis, hepatic granuloma; worldwide; parasite of herbivores, man being infected occasionally from watercress infected by sheep and buffalo; treatment: bithionol

F.gigantica: giant liver fluke; causes fascioliasis (rare), biliary cirrhosis

F.hepatica: sheep liver fluke; 0.04% in travellers from tropics; causes fascioliasis (sheep liver fluke disease (usually acquired by eating raw infected watercress; mainly Latin America, Portugal, Spain; also France, North Africa, UK), adult hepatitis, enteritis, biliary cirrhosis, ? also pharyngeal fascioliasis ('halzoun') following ingestion of raw or poorly cooked infected animal liver); diagnosis: ova in faeces, biliary drainage, duodenal drainage

Fasciolopsis buski: giant intestinal fluke; causes fasciolopsiasis (Busk's fluke infection, giant intestine fluke infection, intestinal distoma, intestinal distomatosis, intestinal distomiasis; enteritis acquired by eating certain aquatic plants bearing encysted metacercariae; 2 M infected worldwide); diagnosis: ova and sometimes adults in faeces, ELISA; treatment: hexylresorcinol, bithionol

Suborder Paraphistomata
Superfamily Paraphistomatoidea
Family Paraphistomidae
Gastrodiscoides hominis: causes gastrodiscoidiasis (gastrodisciasis); fluke attaches itself to caecum and ascending colon; manifested by mucosal inflammation and diarrhoea
Order Opisthorchiida
Suborder Opisthorchiata
Superfamily Opisthorchioidea
Family Heterophyidae
Centrocestus formosanus: found in intestine of man on rare occasions
Haplorchis pumilio: causes intestinal disease in man on rare occasions
H.taichui: causes intestinal disease in man on rare occasions
Heterophyes: causes heterophyiasis (dwarf fluke infection, heterophydiasis, heterophyidiasis; intestinal disease (enteritis) acquired from eating raw or inadequately cooked infected fresh-water fish; occasionally, eggs enter bloodstream and produce granulomatous foci in other tissues, especially brain and myocardium)
Metagonimus: causes metagonimiasis (intestinal disease (enteritis) clinically resembling heterophyiasis, acquired from eating raw or inadequately cooked fresh-water fish)
M.yokogawai: usual cause of metagonimiasis (Yokogawa's fluke infection)
Pygidiopsis summa: 1 report of large numbers from small group of patients in Korea
Stellantchasmus falcatus: causes intestinal disease in man on rare occasions
Family Opisthorchiidae
Clonorchis sinensis: causes clonorchiasis (Chinese liver fluke disease, clonorchiosis, *Clonorchis* liver infection, oriental liver fluke disease; chronic disease of bile ducts acquired from eating raw or inadequately cooked fresh-water fish), biliary cirrhosis, cholangitis and cholecystitis, enteritis; adults in bile ducts; in 2% of Indochinese refugees; diagnosis: ova in stools, bile or biliary drainage; treatment: praziquantel, chloroquine phosphate
Opisthorchis: causes opisthorchiasis (disease of bile ducts acquired by eating raw or inadequately cooked infected fresh-water fish; 1% of SE Asian refugees; diagnosis: ova in stools, biliary drainage, duodenal drainage; treatment: praziquantel, chloroquine phosphate
O.felineus: causes opisthorchiasis (cat liver fluke fever), biliary cirrhosis, cholangitis and cholecystitis
O.viverrini: causes opisthorchiasis, biliary cirrhosis, cholangitis and cholecystitis
Order Plagiorchiida
Suborder Plagiorchiata
Superfamily Plagiorchioidea
Family Dicrocoeliidae
Dicrocoelium: lancet fluke; causes dicrocoeliasis (dicrocoeliiasis, lancet fluke infection); uncommon disease of bile ducts acquired by ingesting second intermediate host, ant of genus *Formica*; transient eggs without infection common in stools in endemic areas)
D.dendriticum: causes dicrocoeliasis, enteritis
D.hospes: causes dicrocoeliasis, enteritis
Family Plagiorchiidae
Plagiorchis muris: reported once from intestinal disease in man
Suborder Troglotremata
Family Nanophyetidae: small troglotromatid flukes related to Paragonimidae; infect members of Canidae and humans in N W USA and Siberia
Nanophyetus salmincola: USA; parasite of salmon; causes salmon-poisoning disease of canines on Pacific coast contracted by eating raw salmon; 10 cases in humans from eating raw, smoked or incompletely cooked salmon or steelhead trout; diagnosis: ova in faeces; treatment: niclosamide, bithionol
Skrjabinophytus neomidis: Siberia; causes nanophyetiasis
Family Paragonimidae
Paragonimus: oriental lung fluke; Asia, W Africa and Central S America; causes paragonimiasis (endemic haemoptysis, lung fluke disease, parasitic haemoptysis, pulmonary distomiasis; pneumonia); larvae invade various organs of body, especially lungs, where granulomatous reaction with development of fibriotic encapsulation occurs; do not grow fully in human body but migrate, especially in chest region, and often cause spontaneous pneumothorax as a result of penetration through visceral pleura; some species localise preferentially in subcutaneous nodules or in CNS, in which case there are no pulmonary findings; treatment: praziquantel, bithionol
P.africanus: causes pulmonary paragonimiasis
P.heterotremus: causes cutaneous paragonimiasis

P.iloktsuenensis: causes pulmonary paragonimiasis
P.kellicotti: causes pulmonary paragonimiasis
P.mexicanus: causes pulmonary paragonimiasis
P.miyazakii: causes pulmonary paragonimiasis
P.ohirai: causes pulmonary paragonimiasis
P.westermani: most frequent cause of pulmonary paragonimiasis, also causes enteritis; diagnosis: ova in faeces and sputum, complement fixation test

Order Strigeidida

Superfamily Schistosomatoidea

Family Schistosomatidae

Austrobilharzia: causes cercarial dermatitis
Gigantobilharzia: causes cercarial dermatitis
Heterobilharzia americana: causes cercarial dermatitis
Orientobilharzia: causes cercarial dermatitis
Schistosoma: blood flukes; most parts of Africa, N and N E S America, Caribbean, Middle East; causes schistosomiasis (bilharziasis, haemic distomiasis, snail fever; 200 M infected worldwide; 75 000 deaths/y worldwide), adult hepatitis, hepatic abscess, 25 of hepatic granuloma; causes diarrhoea by mucosal inflammation, ? hypersensitivity, erosion, ulceration, fibrosis, altered motility of colon; loss of trace elements or vitamins, especially albumin-bound ones (eg., zinc, vitamin A), low D-xylose excretion, elevated faecal fat, glucose intolerance and subnormal levels of serum carnitine occur with heavy infection; transmission from snail by penetration of cercariae through skin; cercariae in papular lesions of skin; inhibits phagocytic recognition; diagnosis: ova in faeces, urine, aspirate, puncture, rectal or colonic granulomas, bentonite flocculation test, complement fixation test, counterimmunoelectrophoresis, fluorescent antibody staining of serum, indirect haemagglutination titre, FAST-ELISA; treatment: niridazole, sodium stibogluconate, praziquantel
S.bovis: causes cercarial dermatitis
S.haematobium: high global prevalence (8% in Chad); Africa, Middle East; causes schistosomiasis (bilharziasis tropical haematuria, bilharziasis of the bladder, bladder schistosomiasis, endemic haematuria, Egyptian haematuria, genitourinary bilharziasis, genitourinary tract schistosomiasis, urinary bilharziasis, urinary schistosomiasis, vesical bilharziasis, vesical schistosomiasis, pulmonary schistosomiasis (very rare), Katayama syndrome (primary; rare)); daily blood loss from bladder 23 mL, daily iron loss 7 mg; cercariae penetrate skin or mucous membranes and migrate via bloodstream to veins of bladder; adults attached to walls of vesical, pelvic and portal blood vessels, eggs discharged in bladder and, less frequently, rectum, genital organs and lungs; also found in liver and spleen parenchyma; treatment: trichlorofon, niridazole, sodium stibogluconate, bicanthone, metrifonate ± praziquantel
S.intercalatum: causes schistosomiasis (enteritis; similar to, but milder than *S.mansoni*); worms and eggs in mesenteric portal system, vesical system not involved, mainly colonic and rectal involvement
S.japonicum: high global prevalence; Japan, China, Philippines; causes acute or chronic schistosomiasis (Asiatic bilharziasis, Asiatic schistosomiasis, eastern schistosomiasis, Hankow fever, hepatic schistosomiasis, Japanese schistosomiasis, Katayama disease, Katayama fever, Kinkiang fever, oriental bilharziasis, oriental intestinal schistosomiasis, oriental schistosomiasis, schistosomiasis japonicum, urticarial fever, Yangtze Valley fever; primarily of intestinal tract (enteritis) and liver, also CNS, Katayama syndrome (primary and secondary), very rarely pulmonary schistosomiasis); adults attached to walls of mesenteric and intrahepatic portal blood vessels and in submucosal blood vessels of large intestine, eggs in liver and spleen parenchyma and, rarely, in brain parenchyma, myocardium and pulmonary arteries; treatment: praziquantel, niridazole
S.mansoni: moderately high global prevalence (36% in Chad, 2% of African refugees, 0.2% of travellers from tropics); Africa, Middle East, S America, Caribbean; causes acute or chronic schistosomiasis (bilharzial dysentery, colon schistosomiasis, Egyptian splenomegaly, intestinal bilharziasis, intestinal schistosomiasis, Manson disease, Manson intestinal schistosomiasis, schistosomal dysentery, schistosomiasis mansoni, visceral schistosomiasis, appendicitis, CNS schistosomiasis, enteritis, Katayama syndrome (primary and secondary), pulmonary schistosomiasis); low overall morbidity; impact on nutrition with symptomatic clinical disease (obstruction of intestinal lymphatics; daily blood loss from gastrointestinal tract 13 mL, daily iron loss 4 mg, daily albumin loss 2.2 g); possible clinical antagonism by malnutrition (severe protein-calorie deficiency depresses egg production, impairs egg maturation and diminishes egg viability; severe protein deficiency exacerbates anaemia and ascites; severe calorie deficiency exacerbates chronic phase low serum albumin, damage to hepatocyte, hepatomegaly, splenomegaly, ascites and portal hypertension, but ameliorates acute phase low serum albumin, damage to hepatocyte, hepatomegaly, splenomegaly and portal hypertension and reduces mortality in chronic phase; calorie, protein, vitamin C, riboflavin, thiamine and pyridoxine deficiency all inhibit granuloma formation); adults attached to walls of intrahepatic portal and mesenteric blood vessels and in submucosal blood vessels of large intestine, eggs in wall of large intestine, in liver, lung and spleen parenchyma and, rarely, present in brain parenchyma; antigenic mimicry by incorporation of host 'self'

antigens into parasite surface; antigenic depletion by shedding of integument; humoral and cellular immunosuppression; targeted chemotherapy moderately feasible, moderate to high priority; treatment: oxamniquine, praziquantel
S.mattheei: causes schistosomiasis (cercarial dermatitis, enteritis)
S.mekongi: causes schistosomiasis (acute or chronic; primarily of intestinal tract and liver; acquired only in Mekong River basin); treatment: praziquantel
S.spindale: causes cercarial dermatitis
Schistosomatium douthitti: causes cercarial dermatitis
Trichobilharzia: causes cercarial dermatitis
Class Heterolobosea
Order Schizopyrenida
Famly Vahlkampfiidae
Naegleria: causes amoebic meningoencephalitis, nonpyogenic meningitis; enters by penetration of mucous membranes; growth stimulated by excess iron
N.australiensis: not isolated from human infections
N.fowleri: causes naegleriasis (acute, fulminant, usually rapidly fatal meningoencephalitis usually affecting children and young adults exposed to water harbouring amoebae ('indigenous' to warm water); gains access to brain via olfactory epithelium); treatment: amphotericin B + miconazole + rifampicin
N.gruberi: not isolated from human infections
N.jadini: not isolated from human infections
N.lovaniensis: not isolated from human infections
Vahlkampfia: associated with corneal infections
Tubulinea
Euamoebida
Tubulinida
Family Hartmanellidae
Hartmanella: associated with corneal infections
Parabasalidea
Class Trichomonada
Order Trichomonadida: trichomonads; axostyle, 1 or 2 blepharoplasts and 3-6 flagella, 1 of which is a trailing flagellum
Family Monocencomonadidae
Dientamoeba: minute; generally 2 nuclei present; central particulate karyosome with several distinct granules; no peripheral chromatin; no cystic stage
D.fragilis: trophozoites 5-15 μm (usual range 9-12 μm), pseudopodia angular, serrated or broad-lobed and hyaline, almost transparent, 2 nuclei (only 1 present in ≈ 20%), invisible in unstained preparations, central granular karyosomes (large cluster of 4-8 granules) and no peripheral chromatin, cytoplasm finely granular, vacuolated, contains bacteria; cysts unknown; prevalence + (14% of immigrant children, 3% of travellers from tropics, 0.9% of homosexual men); pathogenicity ? (noninvasive, but has been associated with low grade superficial irritation of bowel mucosa, excess mucus and recurrent episodes of diarrhoea in 43-58% of cases (10-23% bloody, mucoid or loose stool), abdominal discomfort and pain in 46-54%, flatulence in 6-20%, fatigue and weakness in 6-13%, nausea or vomiting in 4-20%, alternating diarrhoea and constipation in 4-14%, weight loss in 3-10%); chief cause of parasitic gastrointestinal disease in Canada and Great Britain; faecal-oral transmission; trophozoites free in lumen of large intestine, possibly in tissue, found most commonly in mucous secretions within glandular crypts; diagnosis: stained trophozoites: high percentage of binucleate trophozoites, nuclei with peripheral chromatin, 4-8 chromatin granules in central mass; treatment: iodoquinol 650 mg 3 times a day (child: 40 mg/kg daily) for 10 d, tetracycline 250 mg four times a day for 7 d, paromomycin 500 mg 3 times a day for 5-7 d
Family Trichomonadidae: cyclostome, 3-5 free flagella and an additional flagellum on the margin of an undulating membrane, and an axostyle which usually protrudes through posterior end of the body
Subfamily Trichomonadinae
Pentatrichomonas hominis: cosmopolitan; prevalence + (0.1% of travellers from tropics); causes infection in abnormal host; trophozoites free in lumen of large intestine (trichomoniasis, cercomoniasis, intestinal trichomoniasis, intestinal tricomoniasis; no specific signs or symptoms and no conclusive evidence of pathogenicity); diagnosis: unstained trophozoites characteristic motility, undulating membrane, axostyle protruding through posterior part of body, stained trophozoites costa and axosytle, no cysts
Trichomonas: trophozoites with 4 free flagella and fifth along outer margin of an undulating membrane, costa at base of undulating membrane, conspicuous axostyle; causes trichomoniasis (trichomonosis, tricomoniasis), meningitis (associated with surgery)
T.tenax: normal flora of oral cavity of persons with poor oral hygiene; causes an extremely rare disease of mouth, gums and, occasionally, respiratory tract; has been associated with lung or thoracic abscesses

T.vaginalis: flagellate; normal flora of anterior urethra, vagina; prevalence +++; causes trichomoniasis (genital infection in both sexes; trichomonal vaginitis, urogenital *Trichomonas* infection, urogenital trichomoniasis, urogenital *Trichomonas* infection, urogenital tricomoniasis, vaginal trichomoniasis, vaginal tricomoniasis; leucorrhoea, prostatitis, urethritis, vaginitis, vulvovaginitis); sexually (usually) and nonsexually transmitted; often asymptomatic; disease worse in female; infection generally confined to epithelial surface of urogenital tract (trophozoites on surface of vaginal mucosa, in prostatic and seminal fluid in male, in urine of male and female); treatment: metronidazole, clotrimazole, tinidazole, nimorazole, natamycin, crystal violet

Coelomata
Deuterostomia
Phylum Chordata
Subphylum Craniata
Vertebrata
Superclass Gnathostomata: jawed vertebrates
Telestomi
Euteleostomi
Class Actinopterygii
Actinopteri
Neopterygii
Telesotei
Elopocephala
Clupeocepahla
Otocephala
Ostariophysi
Otophysi
Siluriphysi
Order Siluriformes: catfishes
Family Cetopsidae: whalelike catfishes
Cetopsis candiru: vermiform spined fish ('candiru') of Amazon basin; invades rectum, urethra and vagina of bathers
Hemicetopsis candiru: vermiform spined fish ('candiru') of Amazon basin; invades rectum, urethra and vagina of bathers
Protostomia
Annelida/Echiura/Pogonophora Group
Phylum Annelida
Clitellata
Class Hirudinida: leeches
Subclass Hirudinea
Order Arhynchobdellida
Suborder Hirudiniformes
Family Haemadipsidae
Haemadipsa picta: leech; causes external hirudinasis
H.sylvestris: leech; causes external hirudinasis
H.zeylanica: leech; causes external hirudinasis
Family Hirudinidae
Limnatis nilotica: leech; causes internal hirudinasis, laryngeal and tracheal hirudinasis ('halzoun')
Philobdella: leech; causes external hirudinasis
Panarthropoda
Phylum Arthropoda
Class Arachnida
Subclass Acari: cause acarine dermatitis
Superorder Acariformes
Sarcoptiformes
Order Astigmata
Superfamily Acaroidea
Family Acaridae
Subfamily Acarinae
Tyrophagus: from foods; causes pruritic rash
T.longior: causes dermatitis; also reported from urinary tract

T.putrescentiae: causes dermatitis (cheese itch, copra itch, grocer's itch); also reported from urinary tract
Superfamily Glycyphagoidea
Family Glycyphagidae
***Glycyphagus domesticus*:** burrows under skin of man and produces temporary pruritus (grocer's itch)
Psoroptidia
Superfamily Analgoidea: feather mites
Family Pyroglyphidae: house-dust mites
Subfamily Dermatophagoidinae
Dermatophagoides farinae: house dust mite; causes pruritic rash and other allergic reactions
D.pteronyssinus: house dust mite; causes pruritic rash and other allergic reactions
Superfamily Sarcoptoidea
Family Sarcoptidae
Subfamily Sarcoptinae
Family Sarcoptidae
Sarcoptes scabei: causes scabies; treatment: benzyl benzoate, lindane, permethrin
Trombidioformes
Suborder Prostigmata
Anystina
Eleutherengona
Heterostigmata
Superfamily Pyemotoidea
Family Pyemotidae
Pyemotes: burrows under the skin of man and causes dermatitis (grain itch)
Raphignathae
Superfamily Chelyetoidea
Family Demodicidae: follicle mites
Demodex folliculorum: causes blepharitis and dermatitis
Parasitengona: velvet mites
Superfamily Trombiculoidea
Family Trombiculidae: chiggers
Leptotrombidium akamushi: causes trombiculosis
Superorder Parasitiformes
Order Ixodida: ticks
Superfamily Ixodoidea
Family Argasidae: softbacked ticks
Ornithodorinae
Ornithodoros coriaceus: Pajaroello tick; southern USA and Mexico
Ornithodoros moubata: African hut tampan; eastern and southern Africa
Family Ixodidae: hardbacked ticks
Subfamily Amblyomminae
Amblyomma americanum: Lone Star tick; southern and eastern USA; vector of ehrlichiosis, tularemia; causes tick paralysis
Amblyomma ovale: causes tick paralysis
Subfamily Ixodinae
Ixodes holocyclus: Australian paralysis tick; Australia; causes tick paralysis
Ixodes pacificus: western black-legged tick; western USA; vector of Lyme disease, babesiosis; causes tick paralysis
Ixodes ricinus: sheep tick; Europe; vector of Lyme disease, babesiosis
Ixodes scapularis: black-legged tick; northeastern and eastern USA; vector of Lyme disease, babesiosis; causes tick paralysis
Subfamily Rhipicephalinae
Dermacentor andersoni: Rocky Mountain wood tick; southern and western USA; vector of tularemia; causes tick paralysis
D.variabilis: American dog tick; southern and eastern USA; vector of Rocky Mountains spotted fever, tularemia; causes tick paralysis
Rhipicephalus sanguineus: brown dog tick; Australia, Europe, USA

Order Mesostigmata
Monogynaspida
Suborder Dermanyssina
Superfamily Dermanyssoidea
Family Dermanyssidae
***Dermanyssus gallinae*:** chicken mite, fowl mite; causes dermatitis closely resembling scabies
Family Macronyssidae: tropical fowl mites
Ornithonyssus sylvarum: Northern fowl mite; causes dermatitis
Mandibulata
Pancrustacea
Subphylum Crustacea
Crustacea Incertae Sedis
Subphylum Pentastomida: tongue worms
Order Porocephalida
Family Armilliferidae
Armillifer armillatus: pentastome; Middle East; occasionally parasitises man (viscera and eye); usually asymptomatic
Family Linguatulidae
Linguatula serrata: tongue worm; Middle East; causes linguatulosis (intestine, lung, nasopharyngeal region (halzoun), eye (with visual damage), other organs; uncommon), hepatic granuloma; treatment: levamisole
Family Porocephalidae
Porocephalus crotali: causes porocephaliasis (porcephalosis, porocephalosis); infection of human viscera (usually lung or liver); larvae encyst and calcify without producing clinical symptoms but congestion has been noted in pulmonary disease
Superclass Hexapoda
Class Insecta
Dicondylia
Pterygota: winged insects
Subclass Neoptera
Infraclass Endopterygota
Order Coleoptera
Suborder Polyphaga
Infraorder Scarabeformia
Superfamily Scarabaeoidea
Family Scarabaeidae: scarab beetles; cause scarabiasis (canthariasis; infestation, usually of gastrointestinal or urinary tract, by both larval and adult beetles; nose and eye also infested on rare occasions; may be severe irritation of organs involved)
Order Diptera
Suborder Brachycerca
Infraorder Muscomorpha
Eremoneura
Cyclorrhapha
Aschiza
Superfamily Platypezoidea
Family Phoridae: humpbacked flies
Subfamily Metopininae
Tribe Megasaliini
Megaselia: causes myiasis
Superfamily Syrphoidea
Family Syrphidae: hover flies
Subfamily Eristalinae
Tribe Eristalini
Eristalis tenax: causes intestinal myiasis
Schizophora
Acalyptratae
Superfamily Tephritoidea
Family Piophilidae: skipper flies

Subfamily Piophilinae
Family Piophilidae
Piophila: causes genitourinary and intestinal myiasis
Calyptratae
Superfamily Muscoidea
Family Fanniidae
Fannia canicularis: causes intestinal myiasis
Family Muscidae: house flies
Subfamily Muscinae
Tribe Muscini
Musca domestica: causes intestinal and wound myiasis
Superfamily Oestroidea
Family Calliphoridae: blowflies
Subfamily Auchmeromyiinae
Auchmeromyia: causes myiasis
Cordylobia anthropophaga: causes cutaneous myiasis
Subfamily Calliphorinae
Calliphora vicina: causes myiasis
C.vomitoria: causes genitourinary and intestinal myiasis
Cynomya: causes myiasis
Subfamily Chrysomyinae
Tribe Chrysomyini
Chrysomya albiceps: causes myiasis
C.bezziana: causes genitourinary, nasopharyngeal and ocular myiasis
C.chloropyga: causes intestinal and genitourinary myiasis
C.megacephala: causes nasopharyngeal, ocular and wound myiasis
C.putoria: causes genitourinary and intestinal myiasis
Cochliomyia hominivorax: causes cutaneous, nasopharyngeal, ocular and wound myiasis
C.macellaria: causes cutaneous, nasopharyngeal and ocular myiasis
Tribe Phormini
Phormia regina: causes cutaneous and wound myiasis
Subfamily Luciliinae
Lucilia caesar: causes myiasis
L.cuprina: causes wound myiasis
L.sericata: causes nasopharyngeal and wound myiasis
Family Sarcophagidae: flesh flies
Subfamily Paramacronychiinae
Wohlfahrtia vigil: causes cutaneous and wound myiasis
Subfamily Sarcophaginae
Blaesoxipha plinthopyga: causes wound myiasis
Peckia chrysostoma: causes wound myiasis
Ravinia lherminieri: causes intestinal myiasis
Genus *Sarcophaga*
Subgenus *Liopygia*
Sarcophaga crassipalpis: causes wound myiasis
S.ruficornis: causes intestinal and wound myiasis
Subgenus *Liosarcophaga*
S.tibialis: causes wound myiasis
Subgenus *Neobellieria*
Sarcophaga bullata: causes intestinal and wound myiasis
Subgenus *Parasarcophaga*
Sarcophaga albiceps: causes wound myiasis
S.misera: causes wound myiasis
Subgenus *Sarcophaga*
Sarcophaga carnaria: grey flesh fly; causes wound myiasis
S.peregrina: flesh fly; causes intestinal and wound myiasis

Family Psychodidae
Clogmia albipunctata: causes intestinal myiasis
Family Oestridae
Oestrus ovis: causes nasopharyngeal and ocular myiasis
Rhinoestrus purpureus: causes nasopharyngeal and ocular myiasis
Family Hypodermatidae
Hypoderma bovis: causes creeping myiasis, ocular myiasis
H.lineatum: causes creeping myiasis, ocular myiasis
Family Cuteridridae
Dermatobium cyaniventris: causes myiasis
D.hominis: causes cutaneous myiasis
Family Gasterophilidae
Gasterophilus haemorrhoidalis: causes creeping and intestinal myiasis
***G.intestinalis*:** causes creeping, intestinal and ocular myiasis
G.nasalis: causes creeping and intestinal myiasis
Order Siphonaptera: fleas; may cause pruritic rash
Suborder Pulicomorpha
Superfamily Pulicoidea
Family Pulicidae: common fleas
Subamily Tunginae
Tunga penetrans: chigger; causes tungiasis (burrowing flea infestation, chigoe disease, jigger disease, nigua, sandflea infestation)
Infraclass Paraneoptera
Order Phthiraptera: lice
Suborder Anoplura: sucking lice
Family Pediculidae
Pediculus: causes pediculosis
P.humanus: causes blepharitis, pediculosis (head-louse infestation, louse infestation); vector of typhus fever (*Rickettsia prowazeckii*) and relapsing fever (*Borrelia recurrentis*)
Family Phthiridae: pubic lice
Phthirus pubis: causes pthiriasis (crab-louse infestation, phthriasis, phthirosis), blepharitis
Pseudocoelomata
Phylum Acanthocephala: 'thorny-headed worms'; cause acanthocephaliasis (rare infections in man as a result of eating raw fish)
Phylum Nematoda: roundworms; unsegmented; possess mouth, oesophagus and anus; in general, sexes separate; reproduction oviparous or larviparous; infection by ingestion of eggs or penetration of larvae through surfaces or arthropod vector or ingestion of encysted larvae; cause nematosis
Class Chromadorea
Order Ascaridida
Superfamily Ascaridoidea
Family Anisakidae: cause anisakiasis (enteritis); acquired from raw or undercooked infected saltwater fish (herring, cod, tuna, rockfish, salmon, many others) and squid; diagnosis: larvae in faeces and pharynx
Anisakis simplex: causes anisakiasis
Contracaecum osculatum: causes anisakiasis
Pseudoterranova decipiens: cod worm; causes anisakiasis
Family Ascarididae
Ascaris: causes ascariasis (ascaridiasis, ascaridiosis, ascaridosis, ascarisosis, roundworm infection); occurs in soil and water contaminated with animal or human faeces; human-human infection by ingestion of embryonated eggs; migrating larvae pass from small intestine to liver (heavy infection may cause hepatitis and hepatic granuloma) and thence to lungs (heavy infection may cause simple eosinophilic pneumonia—*Ascaris* pneumonia, *Ascaris* pneumonitis), rarely to urogenital tract; treatment: thiabendazole
***A.lumbricoides*:** giant intestinal roundworm; most common helminthic infection worldwide (25% of world's population; 78% of Guatemalan children, 8-9% of immigrants, 3% of SE Asian refugees, 1% of travellers from tropics, up to 90% in parts of India); causes ascariasis—enteritis, appendicitis, cholangitis and cholcystitis, pneumonitis (due to migrating larvae) and, occasionally, visceral larva migrans; 20 000 deaths/y worldwide; faecal-soil (larval development)-oral (eggs) transmission; adults free in lumen of small intestine, larvae in lung parenchyma; low overall morbidity; probable impact on nutrition (biliary obstruction, pancreas obstruction, impaired protein digestion, local irritation and damage and nutrient malabsorption

with heavy load); targeted chemotherapy moderate feasibility, low to moderate priority; treatment: pyrantel embonate, thiabendazole, mebendazole, albendazole, piperazine citrate, praziquantel, vipyrnium embonate, diethylcarbamazine citrate
A.suum: common parasite of pigs; less common cause of ascariasis (enteritis) in man
Baylisascaris procyonis: raccoon roundworm; occasional cause of ocular, visceral and neural larva migrans, 1 case of eosinophilic meningoencephalitis; treatment: thiabendazole, diethylcarbamazine
Toxascaris leonina: a possible cause of visceral larva migrans; treatment: thiabendazole, diethylcarbamazine
Family Toxocaridae
Toxocara: causes hepatic abscess, hepatic granuloma, visceral larva migrans; diagnosis: ELISA, bentonite flocculation, indirect haemagglutination; treatment: thiabendazole, diethylcarbamazine citrate
T.canis: dog ascarid; principal causative organism of visceral larva migrans; also causes anterior uveitis and retinochoroiditis; larvae in brain, liver and lung parenchyma and eye tissue
T.cati: less frequent cause of visceral larva migrans
Order Oxyurida
Superfamily Oxyuroidea
Family Oxyuridae
Enterobius vermicularis: pinworm, seatworm; causes appendicitis (rare), enteritis (relatively common; enterobiasis, enterobiosis, oxyuriasis, oxyuriasis vermicularis, pinworm infection, seatworm infection, threadworm infection), vulvovaginitis in infant girls; peritoneal granulomata reported; infection by ingestion of eggs; intestinal migration; larval development perianal; prevalence up to 20% in parts of India, 10% of travellers from tropics, 0.3% of homosexual men; 500 M infected worldwide; diagnosis: ova in perianal scrapings or sticky tape preparation, occasionally in faeces; treatment: pyrantel embonate, mebendazole, piperazine citrate, pyrvinium pamoate or embonate
Syphacia obvelata: common parasite of rats and mice; found in stools of man but pathogenicity uncertain
Order Rhabditida
Superfamily Panagyrolamoidea
Family Panagroaimidae
Turbatrix aceti: recovered from urine and vaginal exudates but pathogenicity uncertain
Family Strongyloididae
Strongyloides: causes strongyloidiasis (anguillosis, anguilluliasis, anguillulosis, Cochin-China diarrhoea, strongylodiosis), acute diarrhoea and/or vomiting, hepatic granuloma, peritonitis (secondary); non-human species cause cutaneous larva migrans; diagnosis: microscopy for larvae and ova in faeces, serology by indirect fluorescent antibody titre; treatment: thiabendazole, albendazole, ivermectin
S.fuelleborni: causes strongyloidiasis; in infants, disease is more acute than that due to *S.stercoralis* and is often fatal
S.papillosus: may cause cutaneous infections
S.ratti: immunity due to lymphocytes, serum, inflammation and reaginic antibody
S.stercoralis: threadworm; causes strongyloidiasis (enteritis—local irritation and damage and nutrient malabsorption, mucosal damage resulting in endogenous losses; diarrhoea caused by mucosal erosion and ulceration, altered motility, superimposed bacterial infections in small intestine and colon), appendicitis, cutaneous larva migrans, diffuse interstitial pneumonia and pneumonitis (due to migrating larvae), nonpyogenic meningitis, infection in abnormal host (including hyperinfection and disseminated infection in T helper lymphocyte dysfunction); high global prevalence (from 0.2% of US travellers from tropics to 5-50% of SE Asian refugees; 80 M infected worldwide); larval development in soil and intestine; infection by third stage filariform larvae through penetration of skin (often causing urticaria), migrate via bloodstream to lungs (eggs, larvae and adults occasionally in alveoli and bronchial epithelium), sometimes causing respiratory symptoms, then invade intestinal mucosa (parasitic adult females, embryonated eggs and rhabditiform larvae embedded in mucosa of small intestine (not below muscularis mucosae) and in mucus adherent to mucosa); immunity cell-mediated (delayed type hypersensitivity-activated macrophage +++), antibody-dependent cellular cytotoxicity +++, basophil-mast cell ++; if immune response is impaired (eg., in those with AIDS), massive autoinfection may occur, resulting in potentially fatal disseminated disease); diagnosis: indirect fluorescent antibody (titre $\geq$ 1:66), special stain of stool, duodenal aspirate and sputum for ova and parasites; treatment: thiabendazole, pyrantel embonate, mebendazole
Superfamily Rhabditoidea
Family Diploscapteriae
Diploscapter: found in stomach and in urinary tract disease but pathogenicity uncertain
Family Rhabditidae
Subfamily Peloderinae
Pelioditis pellio: found in the vagina; pathogenicity uncertain
Subfamily Rhabditinae
Rhabditis: found in feces; pathogenicity uncertain

Suborder Strongylida

Superfamily Ancyclostomatoidea: hookworms

Family Ancylostomatidae: hookworms; cause enteritis, pneumonitis; high global prevalence (800 M infected worldwide; 3% of immigrant children, 16% of SE Asian refugees, 66% of Laotian immigrants, 0.2% of travellers from tropics, up to 92% in parts of India); 55 000 deaths/y worldwide; larval development in soil; human-human transmission by penetration of skin by, or ingestion of, third stage filariform larvae; pulmonary migration; moderate overall morbidity; impact on nutrition with symptomatic clinical disease (achlorhydria/hypochlorhydria, mucosal damage resulting in endogenous losses); iron supplementation intervention high feasibility and priority; diagnosis: ova and larvae in faeces by brine flotation; treatment: thiabendazole, pyrantel embonate, mebendazole, albendazole, bephenium hydroxynaphtoate, tetrachloroethylene

Subfamily Ancyclostomatinae

Ancylostoma: causes ancyclostomiasis (Wakana disease; chronic disease; larvae penetrate skin (sometimes causing pruritus and itching ('ground itch') and migrate via bloodstream through lungs (where may cause respiratory symptoms) to small intestine; infection by oral route also possible; adult worm attaches itself to, and damages, intestinal mucosa), cutaneous larva migrans (creeping eruption, dermatitis linearis migrans, plumbers itch; larvae penetrate skin and wander for prolonged periods in epidermis, leaving a pruritic trail; larvae unable to complete life cycle as not in 'normal' host; when they die, lesions heal), hepatic granuloma

A.braziliense: causes cutaneous larva migrans; larvae in serpiginous tunnels in stratum germinativum of skin

A.caninum: occasional cause of cutaneous larva migrans

A.ceylanicum: causes ancylostomiasis, cutaneous larva migrans, enteritis

A.duodenale: Old World hookworm; high global prevalence; causes ancyclostomiasis (enteritis; adults attached to mucosa of small intestine) and, occasionally, cutaneous larva migrans

Uncinaria stenocephala: causes cutaneous larva migrans; treatment: thiabendazole

Subfamily Bunostominae

Necator americanus: tropical hookworm; high global prevalence; causes necatoriasis (resembles ancyclostomiasis except initial dermatitis occurs more often and anaemia is usually less severe), enteritis, cutaneous larva migrans; treatment: thiabendazole

Superfamily Metastrongyloidea: lungworms

Family Angiostrongylidae

Angiostrongylus cantonensis: rat lungworm; causes angiostrongyliasis (eosinophilic meningoencepahlitis), eye infections; China, Far East, Hong Kong, Papua New Guinea; treatment: dexamethasone

A.costaricensis: causes angiostrongyliasis (abdominal angiostrongyliasis, abdominal angiostrongyliosis, intestinal angiostrongyliasis, intestinal angiostrongyliosis), appendicitis

A.malaysiensis: causes eosinophilic meningoencephalitis (Malaysia); treatment: dexamethasone + analgesics

Family Metastrongylidae

Metastrongylus elongatus: causes metastrongyliasis (a disease of pigs, reported in man on very rare occasions; affects respiratory tract)

Family Syngamidae: cause syngamiasis (syngamosis; rare disease in which adult worms attach themselves to laryngeal mucosa and cause coughing, haemoptysis and, sometimes, asthma; parasites removed through endoscope)

Superfamily Strongyloidea

Family Chabertiidae

Oesophagostomum: causes oesophagostomiasis (nodular disease); larvae burrow into wall of large intestine and form conspicuous nodules, rupture of which may produce diarrhoea with blood-stained stools, dehydration and, at times, peritonitis

O.bifurcum: causes oesophagostomiasis

O.stephanostomum: causes oesophagostomiasis

Family Strongylidae

Ternidens deminutus: parasite of simian primates; may cause ternidensiasis (cystic nodules found in intestine; severe infections give rise to anaemia) in man

Superfamily Trichostrongyloidea

Family Haemonchidae

Subfamily Haemonchinae

Haemonchus contortus: common parasite of sheep; causes haemonchiasis in man on rare occasions; blood-sucking larvae produce anaemia similar to that found in ancyclostomiasis or necatoriasis

Subfamily Ostertagiinae

Ostertagia ostertagi: common parasite of herbivorous animals; reported from man but pathogenicity uncertain

Teladorsagia circumcincta: common parasite of herbivorous animals; reported from man but pathogenicity uncertain

Family Trichostrongylidae: common parasites of herbivorous animals

Subfamily Trichostrongylinae

Trichostrongylus: causes trichostongyliasis (trichostrongylosis, *Trichostrongylus* infection; enteritis); larvae attach themselves to mucosa of small intestine; diagnosis: ova or adult worms in stool

T.axei: causes trichostrongyliasis

T.columbriformis: common cause of trichostrongyliasis

T.probolurus: causes trichostrongyliasis

T.vitrinus: causes trichostrongyliasis

Order Spirurida

Superfamily Dracunculoidea

Family Dracunculidae

Dracunculus medinensis: dragon worm, medina worm, guinea worm; high global prevalence (20 M; mainly Africa); causes dracunculiasis (dracunculosis, dracontiasis, guinea worm disease, Medina infection, Medina worm infection), 0.8% of carpal tunnel syndrome; transmission from crustacean vector (water fleas or cyclops of many different genera) by ingestion of larvae; gravid female worms migrate to subcutaneous regions; adults in cutaneous lesion; treatment: metronidazole, niridazole, thiabendazole

Superfamily Filaroidea: cause filariasis

Family Onchocercidae

Brugia malayi: Malayan filaria; causes filariasis (Brug filariasis, *Brugia* filariasis, brugiasis, filariasis malayi, Malayan filariasis; lymphangitis, tropical eosinophilic pneumonia); transmitted to man by bite of certain mosquitoes (*Mansonia, Aedes, Anopheles*); microfilaria free in blood, adults in vessels and tissue of lymph node; diagnosis: peripheral thick blood films collected at midnight, histology of biopsy, ELISA, bentonite flocculation, indirect haemagglutination, indirect immunofluorescence; treatment: diethylcarbamazine citrate, ivermectin, flubendazole

B.pahangi: has caused allergic symptoms and tropical eosinophilic pneumonia on rare occasions; treatment: diethylcarbamazine

B.timori: causes filariasis similar to, but often more severe than, that caused by *B.malayi*; transmitted by *Anopheles* mosquitoes in 1 small group of islands in Indonesia; diagnosis and treatment as for *B.malayi*

Dirofilaria: causes dirofilariasis (rare visceral larva migrans); adults in blood vessels and in abscesses or nodules ('coin lesions') in heart, lungs, subcutaneous tissue and eye; treatment: ivermectin, flubendazole

D.immitis: 'cruel' filaria, dog heart worm; causes dirofilariasis (usually lung lesion ('coin lesions')); vectors *Aedes notoscriptus, Culex annulirostris, Aedes vigilax, Aedes camptorhynchus, Culex quinquefasciatus* and *Anopheles annulipes*

D.repens: causes dirofilariasis (may be found in subcutaneous nodules)

Loa loa: loa worm, 'eye worm' causes loiasis (eye worm, eyeworm disease of Africa, loaiasis, loasis, loa worm; eye infection in 5% of cases); 9% prevalence in Chad; vector tabanid flies (*Chrysops silacea* and *Chrysops dimidata*; geographical distribution determines that of the disease); sheathed, diurnal microfilaria in peripheral blood; peripheral microfilaremia increases in response to elevated body temperature; adult worms migrate through subcutaneous tissue and, occasionally, across eye; diagnostic stage in eye and calabar swelling; diagnosis: peripheral thick blood films collected at noon, histology of biopsy, ELISA, bentonite flocculation, indirect haemagglutination, indirect immunofluorescence; treatment: diethylcarbamazine citrate

Mansonella: causes mansonelliasis; transmitted to man by bite of *Culicoides* and, perhaps, *Simulium;* diagnosis: recovery of microfilariae from blood by Knott's concentration (night collection better than day for *M.perstans*); treatment: ivermectin, flubendazole

M.ozzardi: Ozzard's filaria; causes mansonelliasis (filariasis ozzardi, *Mansonella ozzardi* infection, mansonelliasis ozzardi, mansonellosis, Ozzard filariasis

M.perstans: persistent filaria; causes mansonelliasis (acanthocheilonemiasis, dipetalonemiasis due to *Dipetalonema perstans*); 29% prevalence in Chad; microfilaria free in blood, adult worms in abdomen

'M.streptocerca': crooked tail filaria; causes mansonelliasis (dipetalonemiasis due to *Dipetalonema streptocerca*); adults in subcutaneous tissue, microfilariae in skin of upper body; diagnosis: skin snips

Onchocerca volvulus: convoluted filaria; causes onchocerciasis (blinding filariasis, coastal erysipelas, Guatemala nodules, onchocercosis, onchodermatitis, onchopthalmia, river blindness, river disease, river valley blindness, Robles disease; chronic disease of subcutaneous tissue, skin or eye); high global prevalence (92% in Chad); transmitted from blackfly (*Simulium*) vector by penetration of third stage larvae; unsheathed microfilaria in skin and eye, adult worms in subcutaneous tissues; diagnosis: biopsy of nodule, skin shavings, Mazzotti test, radioimmunoassay, patch test; treatment: ivermectin, diethylcarbamazine, suramin, flubendazole

Wuchereria: transmission by bite of mosquito (*Culex, Aedes, Anopheles, Manzonia)* by penetration of third stage larvae

W.bancrofti: Bancroft's filaria; high global prevalence (5% in Chad); causes filariasis (Bancroft filariasis, bancroftian filariasis, bancroftosis, elephantiasis, elephantiasis filariasis, elephantoid fever, wucheriasis; lymphangitis, tropical eosinophilic pneumonia); sheathed, nocturnal microfilaria free in peripheral blood, adult worms infect lymphatic system, most commonly

inguinal area, upper arms, legs, spermatic cord; diagnosis: peripheral thick blood films (collected at midnight), histology of biopsy, ELISA, bentonite flocculation, indirect haemagglutination, indirect immunofluorescence; treatment: diethylcarbamazine, ivermectin, flubendazole

Superfamily Gnathostomatoidea

Family Gnathostomatidae

Gnathostoma: S E Asia and S America; causes gnathostomiasis (gnathomiasis, wandering swelling, Yangtse oedema); larvae invade cutaneous and subcutaneous tissues; cited as occasional cause of visceral larval migrans

G.hispidium: causes infection

G.spinigerum: parasite of a number of carnivores; usual cause of visceral gnathostomiasis, eye infection

Family Physalopteridae

Physaloptera: parasite of simian primates; causes physalopteriasis (enteritis)

Superfamily Thelazioidea

Family Thelazidae

Thelazia: eyeworms; cause thelaziasis (eye worm infection, thelaziosis)

T.callipaeda: causes thelaziasis

Class Enoplea

Subclass Enoplia

Order Mermithida

Superfamily Mermithoidea

Family Mermithidae

Agamermis: recovered from man but pathogenicity doubtful

Order Tricocephalida

Family Trichinellidae

Trichinella pseudospiralis: found in wild animals, not known to cause disease in man

T.spiralis: trichina worm; causes trichinellosis (trichuria worm infection, trichinellasis, trichuriasis, trichinosis, trichinous myositis, trichinous polymyositis), enteritis, nonpyogenic meningitis, encephalitis, maculopapular rash (in 75% of cases), myocarditis and pericarditis (rare); transmitted by ingestion of larvae in raw or inadequately cooked pork and also meat of other animals (wild boar, beaver, rat, horse, badger, bear); transmission of *T.spiralis nativa* in beans has been reported; encysted larvae enter orally, penetrate intestinal mucosa at level of duodenum and jejunum, enter glandular crypts and develop into adults; causes diarrhoea by hypersensitivity reaction in duodenum; adults embedded in mucosa of small intestine and mucus adherent to mucosa (for about 2 mo after inoculation); after mating, females deposit larvae; these reach venules or lymphatics, are distributed throughout body and encyst in striated muscle; 50 M infected worldwide; immunity due to lymphocytes, serum, inflammation, reaginic antibody; diagnosis: ELISA, latex agglutination, immunodiffusion, complement fixation test, indirect haemagglutination, indirect fluorescent antibody (titre $\geq$ 1:16), bentonite flocculation test ($\geq$ +++), muscle biopsy; treatment: mebendazole, albendazole

Family Trichuridae

Anatrichosoma: associated with cutaneous larva migrans on very rare occasions

Capillaria: causes capillariasis, hepatic granuloma

Trichuris: human-human transmission by ingestion of embryonated eggs; 500 M infected worldwide; treatment: mebendazole

T.muris: immunity due to lymphocytes and serum

T.suis: common parasite of pigs; may cause disease in man on rare occasions

T.trichiura: whipworm; causes trichuriasis (trichocephaliasis, tricocephalosis, whipworm disease, whipworm infection; enteritis, appendicitis); causes diarrhoea by intense mucosal inflammation, hyperactivity in caecum and colon; high global prevalence (3% of Guatemalan children, 8% of immigrant children, 12% of Laotian immigrants, 1% of travellers from tropics, up to 94% in parts of India); faecal-soil (larval development)-oral (egg) transmission; adults anterior end embedded in mucosa of large intestine, posterior end free in lumen; diagnosis: ova in faeces; treatment: mebendazole

T.vulpis: common parasite of dogs; may cause disease in man on rare occasions

Phylum Nematomorpha: horsehair worms

Class Gordioida

Order Chordodea

Superfamily Chordodoidea

Family Chordodidae

Chordodes: recovered from man but pathogenicity uncertain

Neochordodes: found in man but pathogenicity uncertain

Order Gordea
Superfamily Gordioidea
Family Gordiidae
Gordius aquaticus: reportedly found in man but pathogenicity uncertain
Paragordius tricuspidatus: found in man but pathogenicity uncertain
P.varius: found in man but pathogenicity uncertain

Part 3: Treatments

Chapter 20

Antivirals

ACICLOVIR: affects replication of DNA by targeting viral DNA polymerase; mode of elimination renal; i.v. (administer slowly), oral (poorly and erratically absorbed from gut but timing with respect to food doesn't matter) and topical (ophthalmic)
Indications: drug of choice for severe *simplexvirus* and *human herpesvirus 3* infections
Side Effects: i.v.: CNS toxicity including encephalopathy and seizures (coma, convulsions; should be administered slowly), crystalluria in renal insufficiency (adjust dose appropriately/increase dosage interval); oral: nausea in 2-8%, headache in 0.6-6%, vomiting, diarrhoea, hallucinations (high dose) common; constipation, abdominal pain, rash, confusion, dizziness, asthenia, agitation, vertigo, arthralgia, renal impairment uncommon; anorexia, fatigue, oedema, leucopoenia, neutropenia rare; dose adjustment needed in renal failure and dialysis; safety in pregnancy not established; interacts with aminoglycosides, amphotericin, cyclosporin, diuretics (especially frusemide; may increase serum concentrations, particularly in patients > 60 y) and vancomycin (monitor renal function due to nephrotoxic potential); increases serum concentrations of probenecid and plasma theophylline levels
VALACICLOVIR: prodrug of aciclovir; improved bioavailability; not affected by food; requires fewer daily doses then aciclovir
Indications: *simplexvirus* and zoster (within 72 h of onset of rash)
Side Effects: as for **ACICLOVIR** but arthralgia, coma, convulsions not reported; safety in pregnancy not established; caution in breastfeeding (insufficient data); dose adjustment required in renal impairment
PENCICLOVIR: similar spectrum to aciclovir
Indications: limited use in treatment of orofacial *simplexvirus*
FAMCICLOVIR: well absorbed from gut (not affected by food); prodrug of penciclovir; requires feweer daily doses then aciclovir
Indications: severe initial genital herpes, zoster, varicella within 24 h of onset of rash
Side Effects: as for **ACICLOVIR** but arthralgia, coma, convulsions not reported; dose interval adjustment required in renal failure and in dialysis
Contraindications: probably safe in pregnancy; avoid if breastfeeding (insufficient data; prefer aciclovir)
VIDARABINE (ADENINE ARABINOSIDE, VIRA-A)
Indications: *simplexvirus* encephalitis and meningitis, *human herpesvirus 3* complications (pneumonitis, encephalitis), mild conjunctivitis and retinochoroiditis due to *simplexvirus*
Side Effects: lacrimation, foreign body sensation, conjunctival injection, burning, irritation, superficial punctate keratitis, pain, photophobia, punctal occlusion, sensitivity
IDOXURIDINE (2′-DEOXY-5-IODORUIDINE, IDU)
Indications: limited topical use in anterior uveitis, mild conjunctivitis and retinochoroiditis due to *simplexvirus* and in cutaneous herpes; in WHO Model List of Essential Drugs
Side Effects: stinging, pruritus, oedema of eye or lids, rare photophobia; probably safe in pregnancy; caution in breastfeeding (insufficient data; prefer aciclovir)
ATROPINE
Indications: *simplexvirus* keratoconjunctivitis and iritis; in WHO Model List of Essential Drugs
Side Effects: rare conjunctival irritation
BENZOCAINE
Indications: pain relief in acute herpetic stomatitis
Side Effects: sensitivity may occur
LIDOCAINE (LIGNOCAINE)
Indications: pain relief in acute herpetic stomatitis
CETYLPYRIDIUM CHLORIDE
Indications: prevention of secondary infection in acute herpetic stomatitis
CHLORHEXIDINE
Indications: prevention of secondary infection in acute herpetic stomatitis
GENTIAN VIOLET (METHYLROSANILINE CHLORIDE): in WHO Model List of Essential Drugs
Indications: prevention of secondary infection in acute herpetic stomatitis
POVIDONE IODINE: in WHO Model List of Essential Drugs

Indications: prevention of secondary infection in acute herpetic stomatitis, genital herpes and zoster
Side Effects: very rare local irritation and sensitivity

Acetaminophen (Paracetamol)
Indications: primary cases of varicella in immunocompetent children < 12 y
Side Effects: potentially fatal liver damage with overdosage

Aspirin (Acetylsalicylic Acid)
Indications: zoster neuralgia (topical), mucocutaneous lymph node syndrome
Side Effects: may cause Reye syndrome by interaction with influenza A, influenza B, varicella-zoster and other viruses

Calamine Lotion
Indications: varicella-zoster (topical)
Side Effects: rare sensitisation

Carbamazepine
Indications: zoster neuralgia
Side Effects: reductions in platelet and white cell counts, bone marrow depression, hepatic effects, skin reactions (including Stevens-Johnson syndrome, Lyell's syndrome), mild anticholinergic activity, dizziness, headache, ataxia, drowsiness, fatigue, diplopia, other neurological effects, isolated cases of psychiatric effects, gastrointestinal disturbances, rare cardiovascular effects, occasional antidiuretic hormone-like effect, disturbances of bone metabolism, rare multi-organ sensitivity, isolated cases of interstitial nephritis and renal failure, lens disturbances, musculoskeletal and respiratory effects;
Contraindications: pregnancy

Saline Packs
Indications: zoster

Interferon Alpha: affects translation by targeting mRNA; s.c. administration; expensive
Indications: hepatitis B, hepatitis C, very frequent recurrences of genital herpes (topical), AIDS (effective in Kaposi's sarcoma; phase I trials in combination with zidovudine show antiviral effect), prophylaxis for upper respiratory infection
Side Effects: thyroid dysfunction, neutropenia, thrombocytopenia, fever, chills, transient bone marrow suppression (increased with zidovudine), myalgia, arthralgia, fatigue, headache, anorexia, weight loss, nausea, vomiting, diarrhoea, dizziness, rash, dry skin, pruritus, partial alopecia, depression in up to 10%, anxiety, decreased mental status (somnolence, forgetfulness, confusion) in up to 30%, change in taste, may cause hepatic decompensation in patients with cirrhosis; decreases theophylline clearance
Contraindications: avoid in moderate to severe renal failure (glomerular filtration rate < 50 mL/min) and in dialysis; severe depression; safety in pregnancy not established

Peginterferon Alpha-2a
Indications: chronic hepatitis C in adults with compensated liver disease

Thymosin Alpha-1: synthetic polypeptide in Phase III trials for treatment of hepatitis C and in Phase II trials for hepatitis B

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors: antiretroviral drugs
Indications: HIV infection
Side Effects: hyperlactatemia, lactic acidosis, hepatic steatosis, lipodystrophy

Zidovudine (Azidothymidine, AZT, ZDV): nucleoside analogue reverse transcriptase inhibitor; inhibits reverse transcription through chain termination; i.v. and oral (not affected by food) administration; penetrates CSF; in Who Model List of Essential Drugs
Indications: treatment and prophylaxis of HIV infection
Side Effects: headache (soon after starting), macrocytic anaemia (uncommon with lower doses), associated malaise, fatigue, dyspepsia, nausea (common), vomiting, bloating, neutropenia (uncommon with lower doses), confusion, nail pigmentation, myalgia, late myositis and congestive cardiomyopathy; 82% develop severe to life-threatening toxic effects (mainly increased haematological toxicity) when treated with zidovudine and ganciclovir concomitantly (may necessitate zidovudine dose reduction or cessation); amphotericin B, flucytosine, interferon, dapsone, i.v. pentamidine, vincristine, vinblastine, adriamycin and doxorubicin also increase haematological toxicity; probenecid, methadone, cimetidine, clofibrate, NSAIDS may increase serum levels and produce toxicity; increased risk of neutropenia and hepatotoxicity with paracetamol; phenytoin decreases levels; ribavirin antagonises antiviral activity; methadone increases area under concentration-time curve by ≈ 40%; may cause opiate withdrawal symptoms in patients on methadone; clarithromycin and rifampicin decrease plasma levels (space 2 h apart); rare reports of profound anemia with lamivudine; lorazepam and oxazepam increase bioavailability; increased risk of neutropenia with vancomycin; dose adjustment required in renal failure and in dialysis
Contraindications: severe pancytopenia; safety in pregnancy not established; avoid if breastfeeding (insufficient data)
Didanosine (2′, 3′-dideoxyinosine, ddI): nucleoside analogue reverse transcriptase inhibitor; oral (take ½ - 1 h before food)

Indications: treatment of HIV; AIDS prophylaxis in significant documented exposure to blood or body fluid containing human immunodeficiency virus from donor on zidovudine > 6 mo
Side Effects: rash/pruritus in 28%, neutropenia in 27%, xerostoma in 25-37%, CNS depression in 23%, increase in haemoglobin ≥ 2 g/dL in 20%, elevation in levels of liver enzymes in 18%, muscle cramps in 17%, diarrhoea in 16-60%, stomatitis in 16%, abdominal pain in 13-25%, joint pain in 11%, hypocalcaemia in 10%, hyperamylasemia in 9-17%, peripheral neuropathy in 8-34% (increased risk with isoniazid, ethambutol, ethionamide, dapsone, phenytoin, metronidazole), nausea/vomiting in 7-25%, headache in 4-35%, constipation in 3-13%, skin rash in 3-12%, asthma in 2-25%, pancreatitis in 2-14% (increased risk with alcohol, i.v. pentamidine), insomnia in 1-25%, optic neuritis, fulminant hepatitis, retinal depigmentation, nausea; in children, elevated uric acid, elevated triglycerides; buffered formulations decrease bioavailability of azithromycin, quinolones, itraconazole capsules, ketoconazole, tetracyclines, dapsone (space doses by 2-3 h); decreased absorption of both didanosine buffered preparations and delaviridine (space 1 h apart); buffered formulations reduce indinavir absorption (space 1 h apart); possible didanosine toxicity with ganciclovir (decreased renal excretion); tenofovir increases plasma levels if taken within 2 h (possible toxicity); methadone decreases area under concentration-time curve by 60%; probably safe in pregnancy; dose interval adjustment required in renal failure and in dialysis
Contraindications: history of pancreatitis, severe peripheral neuropathy; avoid if breastfeeding (insufficient data)
EMTRICITABINE: nucleoside analogue reverse transcriptase inhibitor
Indications: HIV infection
Side Effects: skin discolouration of palms and soles, acute exacerbation of hepatitis B in co-infected patients on discontinuation; probably safe in pregnancy
Contraindications: avoid in brestfeeding (insufficient data)
ZALCITABINE (DIDEOXYCYTIDINE, ddC): nucleoside analogue reverse transcriptase inhibitor; oral (take ½ to 1 h before food)
Indications: may increase CD4 counts in patients with human immunodeficiency virus infection
Side Effects: peripheral neuropathy (increased risk with alcohol, i.v. pentamidine and nephrotoxic drugs including amphotericin, aminoglycosides and foscarnet), stomatitis, mouth ulcers, rash, pancreatitis (rare)
Contraindications: pregnancy; severe peripheral neuropathy; avoid if breastfeeding (insufficient data)
STAVUDINE (D4T): nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)
Indications: HIV/AIDS
Side Effects: peripheral neuropathy (increased risk with alcohol, i.v. pentamidine), pancreatitis; methadone decreases area under concentration-time curve by 18%; ribavirin may reduce effects
Contraindications: severe peripheral neuropathy; safety in pregnancy not established; avoid if breastfeeding (insufficient data)
LAMIVUDINE (3TC): nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)
Indications: HIV/AIDS (may be active against strains resistant to zidovudine), chronic hepatitis b
Side Effects: abnormal liver function, anaemia and neutropenia (advanced disease), pancreatitis (primarily in children), may cause severe and fatal exacerbation of hepatitis B infection if resistance develops or in co-infected HIV/hepatitis B patients on discontinuation; rare reports of profound anaemia with zidovudine; safety in pregnancy not established; reduce dose in impaired renal function
Contraindications: avoid if breastfeeding (insufficient data)
ABACAVIR: carbocyclic nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)
Indications: HIV/AIDS
Side Effects: potentially fatal HLA-linked hypersensitivity reactions (fever, headache, myalgia, gastrointestinal symptoms, respiratory symptoms, with or without rash); safety in pregnancy not established
Contraindications: avoid if breastfeeding
TENOFOVIR DISOPROXIL FUMARATE: nucleotide analogue reverse transcriptase inhibitor; oral; take with or after food (increases bioavailability); once daily dosing
Indications: HIV/AIDS
Side Effects: nephrotoxicity, nausea, vomiting, flatulence, diarrhoea, asthenia, headache, hypophasphataemia, renal impairment (rare), acute exacerbation of hepatitis B in co-infected on discontinuation; increased plasma levels of didanosine if taken within 2 h (possible toxicity); safety in pregnancy not established
Cotnraindications: avoid in breastfeeding (insufficient data)
NON-NUCLEOSIDE ANALOGUE REVERSE TRANSCRIPTASE INHIBITORS
Indications: HIV/AIDS (in combination with nucleoside analogue reverse transcriptase inhibitors)
Side Effects: skin rash, abnormal liver function, fever
NEVIRAPINE: non-nucleoside analogue reverse transcriptase inhibitor; oral (timing to food does not matter)
Indications: HIV/AIDS

Side Effects: hepatotoxicity (especially women with CD4 count > 250/μL and men with CD4 count > 400/μL) , skin reactions (including Stevens-Johnson syndrome), fever; decreases saquinavir levels by 27%, indinavir by 28%, also amprenavir and lopinavir (increased metabolism); decreases caspofungin plasma levels; ketoconazole increases levels while ketoconazole levels are lowered; rifampicin and St John's wort decrease levels; may induce metabolism of voriconazole while voriconazole may inhibit metabolism of nevirapine; precipitates symptoms of narcotic withdrawal in methadone recipients, requiring ≈ 45% increase in dose; safety in pregnancy not established
Contraindications: treatment with ketoconazole, rifampicin, St John's wort; avoid if breastfeeding (insufficient data); not recommended for post-exposure prophylaxis
LOVIRIDE: non-nucleoside analogue reverse transcriptase inhibitor
Indications: HIV/AIDS
DELAVIRDINE: non-nucleoside analogue reverse transcriptase inhibitor; high pill burden; relation to food does not matter
Indications: HIV/AIDS
Side Effects: rash (including Stevens-Johnson syndrome), abnormal liver function, fever; increases saquinavir levels by 3-6 fold; decreases metabolism of alprazolam, midazolam and triazolam (may cause prolonged sedation or respiratory depression), cisapride (may lead to QT interval prolongation), clarithromycin, amprenavir, saquinavir and indinavir (may increase toxicity); interacts with didanosine buffered preparations to decrease absorption of both drugs (space 1 h apart); increases risk of ergotism with ergot derivatives; H_2-receptor antagonists and proton pump inhibitors may reduce absorption by increasing gastric pH; interacts with nelfinavir to increase nelfinavir levels (may cause neutropenia) and decrease delavirdine levels; rifampicin and rifabutin markedly decrease delavirdine effect (increased metabolism) and increase rifamycin toxicity (decreased metabolism); St John's wort decreases levels; interacts with voriconazole to increase plasma levels of both drugs; safety in pregnancy not established
Contraindications: < 12 y old; treatment with cisapride, (dihydro)ergotamine, H_2-receptor antagonists, midazolam, proton pump inhibitors, rifabutin, rifampicin, simvastatin, St John's wort, triazolam; avoid in breastfeeding (insufficient data)
EFAVIRENZ: non-nuceloside reverse transcriptase inhibitor; once daily oral (timing to food does not matter)
Indications: component of initial triple therapy regimen for HIV/AIDS
Side Effects: neuropsychological effects (drowsiness, dizziness, disturbed sleep, vivid dreams, impaired concentration, light headedness, abnormal thinking) common but usually settle over few weeks; skin rash, abnormal liver function; decreases plasma levels of amprenavir, caspofungin, indinavir, lopinavir, saquinavir; increases cisapride plasma levels, increasing risk of QT prolongation; increases risk of ergotism with ergot derivatives; decrease metabolism of midazolam and triazolam (may cause prolonged sedation or respiratory depression), increases plasma levels of nelfinavir and ritonavir (efavirenz levels may increase with ritonavir); rifampicin and St John's wort decrease plasma levels; may inhibit or induce voriconazole metabolism, while voriconazole may inhibit metabolism; theoretical interaction with oral contraceptives
Contraindications: pregnancy; avoid in breastfeeding (insufficient data); treatment with cisapride, (dihydro)ergotamine, midazolam, pimozide, St John's wort, triazolam, voriconazole
PROTEASE INHIBITORS
Indications: HIV/AIDS (in combination with 2 nucleoside analogue reverse transcriptase inhibitors)
Side Effects: 40% nausea/vomiting, 40% diarrhoea, 34% weakness, 30% abdominal pain, 24% headaches, 18% lipodystrophy, hyperlipidemia (most common with ritonavir, least common with atazanavir), hyperglycaemia, abnormal liver function; metabolised by cytochrome P450 system, so many potential drug interactions; reduces metabolism of midazolam, triazolam and, to a lesser extent, alprazolam (may cause prolonged sedation or respiratory depression), cisapride, pimozide, amiodarone and lignocaine (increased risk of cardiac arrhythmias), dextropropoxyphene, fentanyl and tramadol (increased risk of adverse opioid effects), synercid (possible toxicity); increased risk of ergotism with ergot derivatives; increases metabolism of pethidine and produces higher norpethidine levels (increased risk of seizures); carbamazepine, phenytoin, phenobarbitone increase metabolism; marked decrease in plasma levels with rifampicin may cause loss of virological response and resistance (avoid combination); increased plasma levels of simvastatin may cause myopathy and rhabdomyolysis; increased plasma levels of sildenafil increases risk of hypotension and priapism; St John's wort decreases plasma levels; interacts with voricoazole to inhibit metabolism of both drugs
ATAZANAVIR: protease inhibitor; always combine with ritonavir if administered with tenofovir or efavirenz
Indications: treatment of HIV infection
Side Effects: hyperbilirubinaemia/jaundice, rash, prolongation of PR interval; probably safe in pregnancy
Contraindications: not approved for use in children; treatment with cisapride, (dihydro)ergotamine, flecainide, midazolam, pimozide, proton pump inhibitors, quinidine, rifampicin, simvastatin, St John's wort, triazolam; avoid in breastfeeding (insufficient data)
FOSAMPRENAVIR: protease inhibitor
Indications: treatment of HIV infection
Side Effects: nausea, vomiting, diarrhoea, rash, perioral paresthesia

Contraindications: not approved for use in children; safety in pregnancy not established; avoid in brestfeeding (insufficient data); treatment with cisapride, diazepam, (dihydro)ergotamine, flecainide, midazolam, pimozide, rifampicin, simvastatin, St John's wort, triazolam

SAQUINAVIR: protease inhibitor; take with or after food (increased absorption with high fat meals)

Indications: treatment of HIV; occupational exposure to HIV

Side Effects: as for **PROTEASE INHIBITORS,** diarrhoea, nausea, abdominal discomfort; discontinuation rate 47%; rifampicin, rifabutin, phenytoin, carbamazepine decrease bioavailability; ketoconazole increases bioavailability; potential for significant interaction (although less so than with other protease inhibitors) with drugs that induce or inhibit hepatic enzyme CYP3A4 (terfenadine, astemizole, cisapride, alprazolam, triazolam, midazolam, erythromycin, diltiazem, nifedipine, verapamil, fluoexetine, fluvoxamine), due to competitive metabolism, especially with antihistamines, leading to possibility of cardiac arrhthymias; interacts with amprenavir to decrease plasma levels of both drugs; dexamethasone decreases bioavailability; clindamycin, delavirdine, grapefruit juice, azithromycin, increase plasma levels, with possible toxicity; efavirenz, nevirapine decrease plasma levels; probably safe in pregnancy

Contraindications: treatment with amiodarone, cisapride, (dihydro)ergotamine, flecainide, midazolam, pimozide, quinidine, rifabutin, rifampicin, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data); not approved for use in children

INDINAVIR: protease inhibitor; take ½ - 1 h before food; almost always combined with low dose ritonavir

Indications: treatment of HIV; occupational exposure to HIV

Side Effects: as for **PROTEASE INHIBITORS**, renal calculus with inadequate fluid intake, hyperbilirubinemia, nausea, interstitial nephritis; discontinuation rate 33%; rifabutin and rifampicin decrease bioavailability; increases rifabutin levels (substitute azithromycin); ketoconazole increases bioavailability; didanosine buffered preparations, grapefruit juice reduce absorption (space 1 h apart); prolongs sedation due to midazolam (substitute propofol); produces arrhythmia with cisapride (substitute metoclopramide) or terfenadine (substitute loratadine); potential for significant interaction with other drugs that induce or inhibit hepatic enzyme CYP3A4 (astemizole, alprazolam, triazolam, diltiazem, erythromycin, nifedipine, verapanil, fluoxetine, fluvoxamine); interaction with clarithromycin may increase mortality; delavirdine decreases metabolism and my increase toxicity; efavirenz, nevirapine decrease plasma levels; interacts with nelfinavir to increase plasma levels of both drugs; safety in pregnancy not established

Contraindications: renal calculi; treatment with amiodarone, cisapride, (dihyro)ergotamine, flecainide, midazolam, pimozide, rifampicin, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data); not approved for use in children

RITONAVIR: protease inhibitor; oral (take with or after food (absorption enhanced)); inhibits cytochrome P450 enzyme system, boosting levels of co-administered protease inhibitor

Indications: treatment of HIV; occupational exposure to HIV

Side Effects: as for **PROTEASE INHIBITORS,** perioral paraesthesia; discontinuation rate 61%; increases saquinavir levels by 30 fold and also other protease inhibitors (may be desired effect); increases rifabutin levels (substitute azithromycin); prolongs sedation due to midazolam (substitute propofol); produces arrhythmia with cisapride (substitute metoclopramide) or terfenadine (substitute loratadine); potential for significant interaction with other drugs that induce or inhibit hepatic enzyme CYP3A4 (astemizole, alprazolam, triazolam, erythromycin, diltiazem, nifedipine, verapamil, fluoxetine, fluvoxamine); interaction with clarithromycin may increase mortality; increased risk of QT prolongation with amiodarone, quinidine; interacts with efavirenz to increase plasma levels of both drugs; increased risk of cardiac arrhythmias with flecainide; safety in pregnancy not established; theoretical interaction with oral contraceptives

Contraindications: treatment with amiodarone, cisapride, (dihydro)ergotamine, flecainide, fluticasone, midazolam, pethidine, pimozide, quinidine, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data)

NELFINAVIR: protease inhibitor; take with or after food to increase absorption and decrease gastrointestinal side effects

Indications: HIV/AIDS

Side Effects: as for **PROTEASE INHIBITORS;** increases rifabutin levels (substitute azithromycin); prolongs sedation due to midazolam (substitute propofol); produces arrhythmia with cisapride (substitute metoclopramide) or terfenadine (substitute loratadine); potential for significant interaction with other drugs that induce or inhibit hepatic enzyme CYP3A4 (astemizole, alprazolam, triazolam, erythromycin, diltimazem, nifedipine, verapamil, fluoxetine, fluvoxamine); interaction with clarithromycin may increase mortality; increased risk of QT prolongation with amiodarone, quinidine; efavirenz increases plasma levels; increases plasma levels of calcium channel blockers; interacts with delavirdine to increase nelfinavir levels (possible neutropenia) and decrease delavirdine levels; interaction with indinavir may increase toxicity of both drugs (decreased metabolism); may reduce caspofungin plasma levels; probably safe in pregnancy; theoretical interaction with oral contraceptives

Contraindications: treatment with amiodarone, cisapride, (dihydro)ergotamine, midazolam, pimozide, quinidine, rifampicin, simvastatin, St John's wort, triazolam; avoid if breastfeeding (insufficient data)

AMPRENAVIR: protease inhibitor; oral (timing to food does not matter)

Indications: HIV/AIDS

Side Effects: as for **PROTEASE INHIBITORS**, rash, perioral paraesthesia; increased diazepam levels may cause prolonged sedation or respiratory depression; efavirenz, nevirapine, dexamethasone decrease plasma levels; delavirdine increases plasma levels; interaction with saquinavir decreases plasma levels of both drugs; increases plasma levels of amlodipine, dapsone, felodipine, quinidine, tacrolimus, tricyclic antidepressants, verapamil; theoretical interaction with oral contraceptives

Contraindications: treatment with cisapride, diazepam, dihydroergotamine, ergotamine, midazolam, pimozide, rifampicin, simvastatin, St John's wort, triazolam

LOPINAVIR: protease inhibitor; oral (take with or after food); supplied as combination with ritonavir

Indications: HIV/AIDS

Side Effects: as for **PROTEASE INHIBITORS,** nausea, vomiting, diarrhoea; efavirenz, nevirapine decrease plasma levels; increased risk of cardiac arrhythmias with flecainide; safety in pregnancy not established

Contraindications: treatment with amiodarone, cisapride, (dihydro)ergotamine, flecainide, fluticasone, midazolam, pimozide, rifampicin, simvastatin, St John's wort, triazolam, voriconazole; avoid in breastfeeding (insufficient data)

ENFUVIRTIDE (T20): HIV entry inhibitor

Indications: HIV infection

Side Effects: injection site reactions, hypersensitivity, increased incidence of bacterial pneumonia

Contraindications: avoid in pregnancy and breastfeeding (insufficient data)

GRANULOCYTE COLONY STIMULATING FACTOR

Indications: appears effective in preventing infectious morbidity and mortality in advanced HIV infection; reduces amputation rate in diabetics with limb-threatening foot infections

Side Effects: medullary bone pain; infrequent arthralgias and myalgias; erythema, swelling, pruritus at site of infection

GANCICLOVIR (DIHYDROMYPROPOXYMETHYLAMINE, DHPG): inhibits replication of viral DNA; i.v., intraocular implants or injections

Indications: prophylaxis and treatment of life- and sight-threatening *human cytomegalovirus* infections in immunocompromised patients, acute meningoencephalitis in AIDS

Side Effects: dose-dependent suppressive effects on rapidly growing cells (bone marrow (neutropenia in 15-42% (manage with granulocyte colony stimulating factor), granulocytopenia, thrombocytopenia in 5-20% (switch to foscarnet if < 25 000)), spermatogonia (rare), germinal layers of skin and gastrointestinal mucosa; increased toxicity in combination with zidovudine and other nucleoside analogues and other bone marrow suppressive agents (adriamycin, amphotericin, dapsone, flucytosine, pentamidine, cotrimoxazole, vinblastine, vincristine) may necessitate dose reduction or cessation of these agents); CNS effects (disorientation, psychosis) in 18%, nausea in 6%, fever in 6%, rash in 6%, anaemia in 5-10%; anorexia, flatulence, seizures, elevated liver enzymes, pain and phlebitis at injection site, sweating, pruritus, increased serum creatinine and urea concentration common; hepatitis, azoospermia; increased risk of didanosine toxicity (decreased renal excretion); increased risk of generalised seizures with imipenem; dosage interval adjustment necessary in renal failure and in dialysis; probenecid may increase serum concentrations and reduce elimination; safety in breastfeeding not established

Contraindications: pregnancy

VALGANCICLOVIR: prodrug of ganciclovir; oral (take with or after food; well absorbed)

Indications: induction and maintenance treatment of *human cytomegalovirus* retinitis (as effective as i.v. ganciclovir), *human cytomegalovirus* prophylaxis in selected solid organ transplant recipients

Side Effects: granulocytopenia in 27%, anaemia in 26%, thrombocytopenia, diarrhoea, nausea, vomiting; others as for **GANCICLOVIR**; overdose can cause fatal bone marrow suppression; dose adjustment required in renal impairment

Contraindications: hypersensitivity, pregnancy, breastfeeding (insufficient data)

CIDOFIVIR: i.v.

Indications: *human cytomegalovirus* infections

Side Effects: nephrotoxicity (give probenecid before and aafter infusion)

Contraindications: pregnancy, moderate to severe renal impairment, co-administration of other nephrotoxic agents

FOSCARNET (TRISODIUM PHOSPHONOFORMATE): inhibits reverse transcriptase; i.v administration; penetrates CSF; synergy with zidovudine

Indications: *human cytomegalovirus* retinitis, aciclovir resistant *simplexvirus* pneumonitis, enterocolitis or oesophagitis when ganciclovir cannot be used or resistance is suspected

Side Effects: headache, thrombophlebitis, nephrotoxicity (acute renal failure; increased risk with aminoglycosides, amphotericin B, aciclovir, i.v. pentamidine, cidofovir, cyclosporin, other nephrotoxic drugs), involuntary muscle contractions, agitation, confusion, hypophosphatemia (in 20-30%) and hyperphosphatemia (in 10-20%), hypocalcaemia (increased risk with i.v. pentamidine, other calcium lowering agents) and hypercalcemia, hypokalemia, hypomagnesaemia, fatigue, nausea (in 25-40%), vomiting, fever, neurologic toxicity, ulceration of genitals, oropharynx, oesophagus, elevated enzymes, elevated creatinine (in 20-30%), tetany, perioral numbness, finger paresthesias, weakness, anaemia, dysuria, dizziness, anxiety, cough, dyspnoea, fatigue, nausea, vomiting, pruritus, rash common; cholestatic liver changes, hepatosplenomegaly, nephrogenic

diabetes insipidus, pulmonary haemorrhage, pneumonitis, granulocytopenia, leucopoenia uncommon; anaphylaxis, seizures rare; dose adjustment required in mild renal failure
Contraindications: safety in pregnancy and breastfeeding not established
ADEFOVIR
Indications: *human cytomegalovirus* infections, viral hepatitis
Side Effects: nephrotoxicity
CIDOFOVIR: i.v.
Indications: *human cytomegalovirus* infections; smallpox, cowpox and vaccinia (investigational)
Side Effects: nephrotoxicity (give with probenecid before and after infusion, but reduce zidovudine dose by 50% on days when cidofovir/probenecid administered (inhibits renal clearance of zidovudine); increased risk with aminoglycosides, amphotericin, foscarnet, i.v. pentamidine, vancomycin, NSAIDS), neutropenia, diarrhoea, anorexia, nausea, vomiting, headache common; asthenia uncommon; retinal detachment, tachycardia rare
Contraindications: pregnancy, breastfeeding (insufficient data), moderate to severe renal impairment, co-administration of other nephrotoxic agents
ENTECAVIR
Indivations: viral hepatitis
AMANTADINE: probably blocks uncoating of virus; mode of elimination renal; oral (take with or after food)
Indications: used to limited extent for influenza A prophylaxis or early treatment; prophylactically gives 30-70% reduction in infection and illness and decreased duration and quantity of virus shedding; less effective in treatment but probably somewhat beneficial; major antigen shift, persons allergic to eggs, unimmunised high risk patient, hospitalised patients and personnel, institutionalised individuals, particularly elderly; started when influenza outbreak has begun in the community; give with vaccine if available; chronic hepatitis c
Side Effects: incidence 10-25% (discontinuation rate 6-14%); nausea, abdominal pain, restlessness, rare psychiatric disturbances, blurred vision, convulsions with large doses, nervousness, headache, difficulty in concentration, dizziness or light-headedness, slurred speech, ataxia, depression, lethargy, insomnia, anxiety, livedo reticularis, ankle oedema, urinary retention, skin rash, vomiting, leucopoenia, congestive heart failure; safety in pregnancy not established; drugs with a stimulant effect on the central nervous system (dexamphetamine, caffeine, benzhexol, benztopine, orphenadrine) may have their effect enhanced; dosage interval adjustment needed in renal failure and in dialysis
Contraindications: babies < 1 y, patients with active convulsive disorders, breastfeeding
Precautions: psychiatric illness, epilepsy, elderly with cerebral atherosclerosis, recurrent asthma, cardiovascular disease
RIMANTADINE: affects assembly of the virion by targeting membrane proteins (ion channel)
Indications: treatment and prophylaxis of influenza A
Side Effects: as for amantadine but uncommon
ZANAMIVIR: neuraminidase inhibitor; inhalation
Indications: uncomplicated acute influenza in > 7 y.o. symptomatic > 2 d; prevention of spread within households
Side Effects: may exacerbate bronchospasm in severe asthmatics (rare); probably safe in pregnancy
Contraindications: avoid in breastfeeding (insufficient data)
OSELTAMIVIR PHOSPHATE: neuraminidase inhibitor; oral (timing to food does not matter)
Indications: influenza A and B prophylaxis (≥ 13 y) and treatment (≥ 1 y)
Side Effects: nausea, vomiting common; recent reports of possibly related bizarre behaviour in some individuals; probably safe in pregnancy
PERAMIVIR: experimental neuraminidase inhibitor; i.v. (single dose)
Indications: influenza
Contraindications: breastfeeding (insufficient data)
RIBAVIRIN: affects processing of RNA transcripts; i.v., oral (timing to food does not matter but consistency required) and aerosol administration; penetrates CSF; broad antiviral spectrum including *respiratory syncytial virus*, *influenzavirus A* and *B*, *parainfluenza virus*, adenovirus
Indications: use currently limited to respiratory syncytial virus infection in infants at high risk for severe or complicated or in whom prolonged illness might worsen underlying chronic disease (aerosol), Lassa fever treatment and prophylaxis, severe measles in immunocompromised, relapsing hepatitis C and acute adenoviral pneumonia; has also been used in hemorrhagic fever with renal syndrome, nephropathica epidemica, rift valley fever prophylaxis, *Phlebotomus* fever prophylaxis, myocarditis and pericarditis due to influenza viruses, and (as aerosol) in influenza A and B, parainfluenza, URTI, croup, acute viral bronchiolitis and bronchopneumonia, pneumonitis
Side Effects: hemolytic anemia, reticulocytosis common; may reduce effects of stavudine; dose adjustment required in renal failure and dialysis
Contraindications: pregnancy (avoid until 6 mo after completion of therapy); avoid in breastfeeding (insufficient data)
PLECONARIL: blocks enteroviral attachment to cellular receptors by occupying key capsid pocket on virus

Indications: severe enteroviral infection in patients with hypogammglobulinema
Side Effects: nausea in 6%, vomiting in 3%, headache in 3%, stomachache in 3%, fatigue in 3%, anorexia in 3%, urinary incontinence in 3%, worsening ataxia in 3%
Palivizumab: IgG monoclonal antibody
Indications: immunoprophylaxis against respiratory syncytial virus in some premature infants
Hydration
Indications: acute bronchiolitis, bronchitis, catarrh, common or feverish cold, croup, epidemic influenza, 'influenza-like illness', laryngotracheitis, tracheobronchitis, URTI
Steam
Indications: acute bronchiolitis and bronchopneumonia, bronchitis, catarrh, common or feverish cold, croup, epidemic influenza, 'influenza-like illness', laryngotracheitis, tracheobronchitis, URTI; recent studies show little benefit
Zinc Gluconate (Lozenges)
Indications: upper respiratory tract infection
Disoxaril
Indications: persistent enteroviral meningitis in agammaglobulinemic individuals
Methisazone
Indications: smallpox
Steroids
Indications: varicella-zoster iridocyclitis (drops)
Corticosteroids
Indications: viral arthritis
Side Effects: usually not significant at dosages and duration of therapy used for this indication
Betamethasone
Indications: acute hemorrhagic conjunctivitis
Side Effects: hypersensitivity
Dexamethasone
Indications: acute pharyngitis, severe croup requiring hospitalisation, *simplexvirus* meningitis
Side Effects: usually not significant at dosages and duration of therapy used for these indications
Prednisolone
Indications: zoster in elderly
Side Effects: usually not significant at dosages and duration of therapy used for this indication; pancreatitis on higher doses or longer exposures
Prednisone
Indications: non-infectious esophageal ulcers in AIDS, viral meningoencephalitis
Side Effects: usually not significant at dosages and duration of therapy used for this indication
Non-steroidal Anti-inflammatory Drugs
Indications: viral arthritis
Side Effects: gastrointestinal effects, tinnitus, oedema, fluid retention, rash, pruritis, dizziness, headache, nervousness, decreased appetite, uncommon congestive heart failure, depression, insomnia, severe skin reactions, rare haematological reactions, hepatotoxicity, gastrointestinal ulceration and hemorrhaging, amblyopia
Cryotherapy
Indications: anorectal, external genital, meatal, oral, perianal and vaginal/cervical warts
Electrosurgery
Indications: anorectal, external genital, meatal, oral, perianal and vaginal/cervical warts
5-fluorouracil: in WHO Model List of Essential Drugs
Indications: urethral warts
Side Effects: causes neutropenia by myelosuppression
Podophyllin (Podophyllum): in WHO Model List of Essential Drugs
Indications: warts other than oral, cervical, rectal, anorectal, urethral or venereal warts in pregnancy
Side Effects: occasional severe discomfort
Contraindications: pregnancy, breastfeeding
Podofilox (Podophyllotoxin)
Indications: anogenital warts (5% gel; 37% clearance)
Side Effects: burning, inflammation, itching, erosion in 29-91%
Contraindications: pregnancy, breastfeeding
Imiquimod: cytokine inducer
Indications: anogenital warts (topical; 50% resolution), erythroplasia of Queyrat

Side Effects: erythema (6% severe, 34% moderate), erosion or oedema in < 1%; safety in pregnancy, breastfeeding and transplant patients not established

Bichloroacetic Acid

Indications: warts

Side Effects: safe in pregnancy and lactation

Contraindications: large areas, friable warts

Trichloroacetic Acid

Indications: warts

Side Effects: safe in pregnancy and lactation

Contraindications: large areas, friable warts

Surgery

Indications: anorectal, external genital, meatal, oral, perianal and vaginal/cervical warts

Thiotepa

Indications: urethral warts

Side Effects: bone marrow depression, allergic reactions

Dietary Restriction

Indications: epidemic viral diarrhoea, viral gastroenteritis

Rehydration

Indications: epidemic viral diarrhoea, viral gastroenteritis, acute diarrhoea and vomiting, traveller's diarrhoea, postnatal gastroenteritis

Immunostimulation

Indications: prophylaxis and treatment of cytomegaloviral diffuse interstitial pneumonia and cytomegalic inclusion disease, viral meningoencephalitis, prophylaxis of varicella-zoster, hepatitis A, hepatitis B, mucocutaneous lymph node syndrome

Levamisole

Indications: used as an immunostimulant (in doses 40-60 times higher than as an antihelminthic) in abnormal monocyte chemotaxis during influenza infection, abnormal neutrophil chemotaxis in *simplexvirus* virus infection, deactivation by chemoattractants, hyper-IgE-recurrent-infection syndrome, hypogammaglobulinemia (IgA deficiency)

Postconvalescent Plasma

Indications: Argentinian hemorrhagic fever

Prostaglandin E_1

Indications: mucocutaneous lymph node syndrome

Volume Replacement

Indications: dengue

Chapter 21

Antibacterials

ANTIBIOTICS: Antibiotics should be used only where the benefits are scientifically demonstrable and substantial. The choice of a particular agent should take into account antimicrobial spectrum, clinical efficacy, safety, previous clinical experience, potential for selecting resistant organisms and associated risk of superinfection, cost, as well as patient factors (including hypersensitivity, age, renal or hepatic impairment). The relative importance of each of these factors will be influenced by the severity of the illness and whether the drug is to be used for prophylaxis, empirical therapy or therapy directed at one or more identified pathogens. As far as possible, therapy should be directed against specific organisms and guided by microbiology. Directed antimicrobial therapy for proven pathogens should use the most effective, least toxic, narrowest spectrum agent available. Choice of parenteral or oral formulations should be determined by the site and severity of infection, with preference for oral therapy wherever feasible. The dosage should be high enough to ensure efficacy and minimise the risk of resistance selection and low enough to minimise the risk of dose-related toxicity. Antibiotic combinations should only be used when it has been proven that such combinations are necessary to achieve efficacy or to prevent the emergence of resistant organisms. Empirical antimicrobial therapy should be based on local epidemiological data on potential pathogens and their patterns of susceptibility. Indications should be evidence-based. Duration of therapy should be as short as possible and should not exceed 7 days unless there is proof that this duration is inadequate. Prophylactic antibiotics should be restricted to a limited range of drugs of proven efficacy in situations where they have been proven to be effective or where the consequences of infection are disastrous. Surgical prophylaxis should be such as to achieve high plasma and tissue levels during, and immediately following, the operation. This will usually be best achieved by parenteral dosing commencing just before the operation. A single dose should be used unless it has been demonstrated that the benefits of longer-term prophylaxis outweigh the risk of resistance selection or propagation. Because of their potent capacity for selecting resistant organisms and the risk of patient sensitisation, topical antibiotics should be restricted to proven indications and topical antiseptics substituted wherever possible. Appropriate specimens for microscopy, culture and susceptibility testing should be obtained before commencing antibacterial therapy. A Gram stain or direct antigen detection may allow specific therapy before the pathogen has been cultured.

BETA-LACTAM ANTIBIOTICS: penicillins, cephalosporins (including cephamycins), monobactams, carbapenems; inhibit transpeptidase, thus preventing cross-linking of cell wall peptidoglycan; active against Gram positive and Gram negative bacteria; bactericidal; activity depends on duration of exposure; induce an increased release of chemoattractants from bacteria; some classes lead to markedly increased levels of free endotoxins

PENICILLIN: kills only growing organisms; no or slight postantibiotic effect; bactericidal; penetrates well into mammalian cells; mainly active against Gram positive bacteria; inactivated by β-lactamases; most active antibiotic against non-enterococcal streptococci; spectrum includes *Actinomyces* (97% susceptible), anaerobic cocci (100% susceptible), anaerobic Gram positive bacilli, *Bacteroides ureolyticus* (MIC ≤ 0.25 mg/L), *Borrelia recurrentis*, *Capnocytophaga canimorsus* (95% susceptible), *Cardiobacterium hominis, Clostridium* (100% susceptible), *Corynebacterium diphtheriae* (resistance not yet confirmed in Australia), *Corynebacterium pseudotuberculosis, Eikenella corrodens* (99% susceptible), *Enterococcus* (in Australia, 2% resistant), *Erysipelothrix* (100% susceptible at 0.06 mg/L), *Eubacterium*, *Fusobacterium* (100% susceptible), *Helicobacter pylori, Listeria* (0.25 mg/L), *Moraxella* (≤ 0.06-0.5 mg/L), *Neisseria gonorrhoeae* (in Australia, 6% resistant due to β-lactamase and 10% chromosomal resistance; 98% total resistance in Vietnam), *Neisseria meningitidis* (in Australia, < 5% MIC > 1 mg/L), *Pasteurella* (resistance not yet confirmed in Australia), penicillinase negative *Staphylococcus aureus* (≤ 0.03 mg/L; 5% of *Staphylococcus aureus* isolated), streptococci including *Streptococcus agalactiae* (< 5% resistance in Australia), *Streptococcus canis* (< 5% resistance in Australia), *Streptococcus* groups C and F (< 5% resistance in Australia), *Streptococcus milleri* (< 5% resistance in Australia), *Streptococcus pneumoniae* (in Australia, 9% intermediate or fully resistant), *Streptococcus pyogenes* (resistance not yet reported), *Treponema pallidum*; Enterobacteriaceae 100% intrinsic resistance, *Moraxella catarrhalis* 85% acquired resistance due to β-lactamase (probably all resistant in clinical practice), *Staphylococcus aureus* 95% acquired resistance due to β-lactamase; shows synergism with monocytes; shows microbicidal activity against bacteria ingested by monocytes or macrophages; no effect on opsonisation, chemotaxis or neutrophil penetration; significant inoculum effect

Indications: clostridial abortional and puerperal infection; actinomycosis; anthrax; bacteremia and septicemia due to *Capnocytophaga canimorsus, Leptotrichia buccalis, Leuconostoc;* acute bronchiolitis and bronchopneumonia; acute bronchitis; cat bites; cellulitis due to *Erysipelothrix rhusiopathiae;* dental infections; dermatophilosis; diphtheria; dog bites; endocarditis due to *Corynebacterium;* erysipelas; erysipeloid; necrotising ulcerative gingivostomatitis; gonorrhoea; hepatic abscess and hepatic granuloma due to *Actinomyces;* hepatitis due to *Staphylococcus aureus* (susceptible strains), *Listeria monocytogenes*, *Treponema pallidum*, *Borrelia recurrentis*, *Actinomyces;* impetigo; ischiorectal abscess; local and generalised sepsis due to

Clostridium botulinum; mastitis; infections (including postneonatal pyogenic meningitis) due to *Pasteurella multocida;* mouth abscess; otitis externa due to *Streptococcus*, *Corynebacterium diphtheriae*, *Actinomyces;* streptococcal and gonococcal peritonitis; peritonsillar abscess; streptococcal and meningococcal pneumonia; streptococcal psoas abscess; rheumatic fever; salivary calculus; scarlet fever; acute maxillary sinusitis; splenic abscess due to *Propionibacterium;* all streptococcal infections; surgical prophylaxis in amputation; syphilis; systemic infection prophylaxis in hyposplenism/splenectomy; tetanus; Vincent's angina

Side Effects: hypersensitivity reactions (1-10%; commonly urticaria, uncommonly angiedema, rarely anaphylactic shock within 72 h; later, urticarial rash (common), fever (uncommon), hemolysis (rare), serum sickness-like reaction (rare); 3-6% cross reaction with cephalosporins; skin test predictive; desensitisation possible), gastrointestinal disturbances (nausea, diarrhoea) with oral preparations, skin reactions (rash, urticaria), pain and inflammation at injection site common; superinfection common with prolonged treatment and/or with broad spectrum penicillins; bronchospasm, vomiting, erythema, toxic epidermal necrolysis, Stevens-Johnson syndrome, colitis uncommon; interstitial nephritis, blood dyscrasias, electrolyte disturbances (potassium metabolic effects), platelet dysfunction and bleeding, haemolytic anaemia, haemolytic uraemic syndrome rare; aseptic meningitis; all penicillins cause neutropenia by myelosuppression; therapeutic efficacy may be decreased by chloramphenicol, tetracycline and erythromycin; serum levels increased and prolonged by probenecid (desired effect); probably safe in therapeutic amounts during pregnancy; modify dosage in severe renal dysfunction (CNS toxicity and aminoglycoside inactivation) and monitor serum levels when possible (maximum permissible blood level 128 mg/L); further dose required after hemodialysis; unpredictable enhanced warfarin effect

Benzylpenicillin (Penicillin G): narrow spectrum (Gram positive) very acid unstable, β-lactamase unstable penicillin; parenteral (i.m. or i.v. 4 times a day); 59% protein binding, no significant change in protein binding in elderly; active against *Enterococcus faecalis*, *Haemophilus influenzae*, *Neisseria meningitidis*, non-β-lactamase-producing *Staphylococcus aureus* (85% of methicillin susceptible strains resistant in Australia), *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus viridans*; *Pseudomonas* 100% intrinsic resistance; *Moraxella catarrhalis* 94% acquired resistance due to β-lactamase (probably all resistant in clinical practice); in WHO Model List of Essential Drugs; mode of elimination renal; incompatible with lincomycin, tetracycline, vancomycin

Indications: treatment of choice for many infections; in i.v. treatment, when high doses required; abscesses; actinomycosis; anaerobic infections; anthrax; septic arthritis (community acquired, due to *Neisseria*, *Kingella kingae*, *Streptococcus*, *Capnocytophaga*, *Arcanobacterium haemolyticum*, *Streptobacillus moniliformis);* bacteremia and septicemia due to *Neisseria meningitidis, Streptococcus pyogenes;* brain abscess from frontal sinuses, ear or mastoid or due to streptococci, *Actinomyces* or anaerobes; severe streptococcal or clostridial cellulitis; cerebrospinal fluid shunt infections; cervical fascial space infections in normal patients; clostridial myositis; compound fractures prophylaxis if wound soiling, severe tissue damage and/or devitalised tissue; purulent conjunctivitis due to *Neisseria*, *Listeria monocytogenes*; diphtheria prophylaxis in close contacts; disseminated gonococcal and meningococcal disease; endocarditis; severe erysipelas; erythema serpens; necrotising fasciitis due to *Streptococcus pyogenes*; gas gangrene; gonorrhoea; meningococcal and streptococcal hemorrhagic fever; acute leptospirosis; *Listeria monocytogenes* prophylaxis in pregnancy; lymph gland infections due to *Corynebacterium pseudotuberculosis;* meningitis (postneonatal pyogenic in adult; streptococcal, gonococcal and listerial in neonate); myocarditis and pericarditis due to *Actinomyces*, *Neisseria meningitidis;* necrotising ulcerative gingivostomatitis; osteomyelitis and osteochondritis due to *Streptococcus*, *Kingella kingae;* streptococcal and clostridial pelvic sepsis; perinatal and prenatal generalised disease due to *Clostridium*, *Corynebacterium*, *Neisseria gonorrhoeae*, *Peptostreptococcus*, *Streptococcus*; peritonsillar abscess in normal host; pharyngitis; pneumonia (severe community acquired in non-tropical Australia, moderate nosocomial with no specific risk factors, aspiration, moderate to severe anaerobic pleuropulmonary, intensive care, pneumococcal, penicillin susceptible staphylococcal, neonatal); pulmonary abscess; rheumatic fever prophylaxis; salpingitis; streptococcal and enterococcal local and generalised sepsis; acute sinusitis; localised skin lesions due to *Streptococcus pyogenes*, *Neisseria*, *Staphylococcus aureus* (susceptible strains), *Clostridium botulinum*; synergistic gangrene; tertiary and congenital syphilis; systemic infections in patients with C5, 6, 7, 8 deficiency; tetanus; acute throat infections due to *Corynebacterium* and *Arcanobacterium haemolyticum*; streptococcal toxic shock syndrome; tubo-ovarian abscess

Side Effects: sensitivity to penicillin, anaphylactic shock in hypersensitive patients; convulsions, bone marrow suppression, megaloblastic marrow, positive direct Coomb's test and associated hemolytic anaemia with very large doses; pain at injection site; requires moderate to significant adjustment of dosage in renal failure (rarely, seizures, interstitial nephritis, sodium overload, hypokalemia) and in dialysis; safe in pregnancy; probenecid increases plasma levels; unpredictable enhanced warfarin effect

Contraindications: penicillin hypersensitivity

Benzathine Benzyl Penicillin: narrow spectrum β-lactamase unstable penicillin; i.m. preparation; provides low levels of benzylpenicillin for up to 4 w; in WHO Model List of Essential Drugs

Indications: severe impetigo with cellulitis in remote areas, Lyme disease arthritis, rheumatic fever prophylaxis and treatment, scarlet fever, syphilis (noncompliant, congenital, late latent, tertiary), acute streptococcal throat infections in remote areas

Side Effects: sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; safe in pregnancy
Contraindications: penicillin hypersensitivity

PROCAINE BENZYL PENICILLIN: narrow spectrum, β-lactamase unstable penicillin; i.m. preparation; daily dose provides adequate levels for up to 24 h against highly susceptible organisms; in WHO Model List of Essential Drugs
Indications: abscess; anthrax; boils; breast abscess; cat and dog bites; less severe streptococcal cellulitis; purulent conjunctivitis due to *Neisseria* in remote areas; diphtheria treatment and carriers; less severe erysipelas; uncomplicated gonorrhoea; human bite and clenched fist injury infections; louse-borne relapsing fever; necrotising ulcerative gingivostomatitis; neurosurgery prophylaxis in CSF leakage; acute otitis media; pelvic inflammatory disease; pericoronitis; mild to moderate community acquired pneumonia; quinsy; rat bite fever; streptococcal local and generalised sepsis; syphilis (late latent and tertiary, HIV infected patients, cardiovascular, neurosyphilis, congenital, prophylaxis); acute streptococcal and gonococcal infections
Side Effects: sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients (epinephrine must be injected at once); safe in pregnancy and breastfeeding
Contraindications: penicillin hypersensitivity; do not use in newborn babies unless no other penicillin or ampicillin is available (in emergencies)

PHENETHICILLIN: Gram positive effective, acid stable, sensitive to β-lactamases; well absorbed; activity equal to phenoxymethylpenicillin
Indication: prophylaxis of recurrent streptococcal infections including rheumatic fever

BICILLIN: benzathine penicillin + procaine penicillin + benzylpenicillin; i.m. single or daily dose
Indications: cat and dog bite infections in remote areas, erysipelas in remote areas, human bite and clenched fist injury infections in remote areas, acute otitis media in remote areas, acute streptococcal throat infections in remote areas
Side Effects: as for components

PHENOXYMETHYLPENICILLIN (PENICILLIN V): narrow spectrum (Gram positive), acid stable, β-lactamase unstable penicillin; may be given orally; well absorbed but absorption impaired by food (take ½ -1 h before food); bioavailability 65%; no significant change in absorption in elderly; 66% protein binding; lower activity than benzylpenicillin against staphylococci (in Australia, 85% acquired resistance due to β-lactamase) and streptococci, low activity against *Haemophilus influenzae*; *Pseudomonas* 100% intrinsic resistance; *Moraxella catarrhalis* 94% acquired resistance due to β-lactamase (probably all resistant in clinical practice); in WHO Model List of Essential Drugs and UNHCR Basic List of Essential Drugs; mode of elimination renal
Indications: actinomycosis; septic arthritis due to *Kingella kingae*; acute bronchitis; less severe cellulitis due to *Streptococcus pyogenes*; diphtheria; streptococcal endocarditis; less severe erysipelas; erythema chronicum migrans; gingival and periodontal infection; impetigo; myocarditis and pericarditis due to *Actinomyces;* necrotising ulcerative gingivostomatitis; osteomyelitis and osteochondritis due to *Streptococcus*, *Kingella kingae*; acute streptococcal otitis media; pericoronitis; pneumococcal pneumonia; rat bite fever; prophylaxis and treatment of recurrent streptococcal infections including rheumatic fever; streptococcal local and generalised sepsis; acute sinusitis; surgical prophylaxis (CSF leakage, postsplenectomy); acute streptococcal throat infections; tooth abscess; streptococcal water-related infections
Side Effects: sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; dosage adjustment not required in renal failure (rarely, seizures); dose after intermittent haemodialysis; safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; probenecid increases plasma levels; very weak association with oral contraceptive failure
Contraindications: penicillin hypersensitivity

PROPICILLIN: potassium salt of phenoxypropylpenicillin; similar to phenoxymethylpenicillin but can be administered with food and has higher bioavailability (85%)

METHICILLIN: antistaphylococcal, β-lactamase stable, acid unstable penicillin; 33% protein binding; higher activity than phenoxymethylpenicillin against β-lactamase-producing *Staphylococcus aureus* and against *Streptococcus pyogenes*; no longer available (replaced by dicloxacillin or flucloxacillin); methicillin resistant *Staphylococcus aureus* should be regarded as clinically resistant to all β-lactams irrespective of laboratory reports of susceptibility
Indications: persistent *Staphylococcus aureus* infection in cystic fibrosis (inhalation)
Side Effects: greater nephrotoxicity than cloxacillin and flucloxacillin

OXACILLIN: Gram positive effective, acid stable, resistant to most β-lactamases; orally absorbed; 92% protein binding; minimal inoculum effect; most active antibiotic against methicillin susceptible staphylococci; lower activity than methicillin against *Streptococcus pyogenes*; low activity against *Enterococcus faecalis*
Indications: endocarditis due to methicillin susceptible *Staphylococcus*, staphylococcal postneonatal pyogenic meningitis, staphylococcal local and generalised sepsis
Side Effects: hepatotoxicity in 22%, rash in 32%; safety not established in pregnancy; dosage modification not required in renal dysfunction

CLOXACILLIN: narrow spectrum and antistaphylococcal, β-lactamase stable, acid stable penicillin; 95% protein binding; orally absorbed (take ½ - 1 h before food) but now only used parenterally; activity equal to oxacillin; minimal inoculum

effect; Enterobacteriaceae and *Enterococcus* 100% intrinsic resistance; in Australia, 22% *Staphylococcus aureus* resistant (mainly confined to teaching hospitals in eastern Australia); mode of elimination renal; in WHO Model List of Essential Drugs; incompatible with erythromycin, gentamicin, polymyxin B, tetracycline

Indications: abscesses; septic arthritis; bacteremia and septicemia (focus probably intravascular catheter); acute bronchiolitis and bronchopneumonia; cellulitis; chondritis; endocarditis due to methicillin susceptible *Staphylococcus aureus;* staphylococcal enterocolitis; *Erysipelothrix rhusiopathiae* infections (100% susceptible at 0.025 mg/L); acute severe furunculosis; staphylococcal hepatitis; impetigo; mastoiditis; meningitis; musculoskeletal trauma prophylaxis; acute neonatal osteomyelitis and osteochondritis; serious ophthalmia neonatorum due to *Staphylococcus aureus*; bacterial parotitis and submandibular sialadenitis; perichondritis; perinatal generalised disease due to *Staphylococcus aureus* (hospital acquired); staphylococcal pneumonia; scalded skin syndrome; skin infections; methicillin susceptible staphylococcal infections (including lymph gland infections, splenic abscess, toxic shock syndrome); symbiotic gangrene

Side Effects: sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; to be given under medical supervision; safe in pregnancy; dosage modification not required in renal dysfunction (rarely, seizures) or dialysis; probenecid increases plasma levels

Flucloxacillin (Nafcillin): narrow spectrum and antistaphylococcal β-lactamase stable penicillin; more readily absorbed by oral route than cloxacillin and may cause less gastrointestinal upset (take ½ -1 h before food, 4 times a day or twice a day with probenecid); also parenteral; Enterobacteriaceae, *Pseudomonas* and *Enterococcus* 100% intrinsic resistance; in Australia, 22% *Staphylococcus aureus* isolates from metro hospitals and 10% of isolates from private laboratories resistant (significant geographic variation); serum protein binding 96%; reduced protein binding and clearance in elderly; mode of elimination renal

Indications: both orally and parenterally, has become treatment of choice for susceptible *Staphylococcus aureus* infections but should not be used for trivial infections; septic arthritis (staphylococcal and organism unknown); bacteremia and septicemia (infection from respiratory system in children, focus probably open skin infection/cellulitis, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer, focus probably intravascular catheter, unidentified source, due to *Staphylococcus aureus*); staphylococcal blepharitis associated with lid abscess; bullous impetigo; staphylococcal cellulitis; compound fractures prophylaxis; endocarditis treatment and prophylaxis; acute mastitis and breast abscess; mastoiditis; osteomyelitis (acute neonatal, due to *Staphylococcus aureus*); acute localised otitis externa; staphylococcal parotitis and submandibular sialadenitis, pneumonia (staphylococcal, severe community acquired in children, mild to moderate nosocomial in patients with diabetes, coma, head injury); preseptal and postseptal cellulitis; local and generalised sepsis (due to *Bacillus cereus*, organism unknown); complicated or severe acute sinusitis; methicillin susceptible staphylococcal infections (including pyoderma with cellulitis or recurrent, toxic shock syndrome); surgical prophylaxis (cardiovascular, vascular grafts, breast, dialysis access, orthopaedic, muscular, skeletal and soft tissue trauma), neurosurgery; symbiotic gangrene; suppurative wound infections

Side Effects: severe, long-lasting cholestasis (rarely fatal), especially in elderly (> 55 y) and if treatment > 14 d (oral or i.v.), after oral or i.v. and up to 6 w after treatment; rash in 10%; adjustment of dosage interval required in renal failure (rarely, seizures) and in continuous venovenous or arteriovenous hemodialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; probenecid increases plasma levels; weak association with oral contraceptive failure; unpredictable enhanced warfarin effect

Flucloxacillin Hydroxyapatite Granules

Indications: staphylococcal osteomyelitis

Dicloxacillin: narrow spectrum and antistaphylococcal; similar to cloxacillin/flucloxacillin; oral (take ½ - 1 h before food) and parenteral; minimal inoculum effect

Indications: serious staphylococcal infections

Side Effects: as for **Flucloxacillin** but less hepatotoxic and more likely to produce thrombophlebitis and interstitial nephritis; high dose may cause diarrhoea; safety in pregnancy not established

Ampicillin: moderate spectrum, very acid stable, β-lactamase sensitive aminopenicillin; oral (take ½ - 1 h before food) and parenteral; well absorbed; mean peak serum concentration 3.7 mg/L after 0.8 mole oral dose; 45% urinary recovery; 3% bronchial penetration 2-3 h after 1 g oral dose; intraperitoneal penetration 96%; protein binding 15-18%; increased interindividual variability in absorption, reduced clearance, no significant change in V_d in elderly; no postantibiotic effect; greater activity than benzylpenicillin against some Gram negative organisms; agent of choice against *Enterococcus* (in Australia, *E.faecalis* 0.7% resistant, *E.faecium* 69% resistant); less active than benzylpenicillin against *Streptococcus viridans*; spectrum includes *Borrelia burgdorferi* (MIC 0.25-1 mg/L), *Brucella*, *Erysipelothrix* (100% susceptible at 0.25 mg/L), *Haemophilus influenzae* (in Australia, 28% resistant), *Listeria monocytogenes* (resistance not yet confirmed in Australia), *Neisseria gonorrhoeae* (in Australia, 15% resistance due to both β-lactamase and altered penicillin binding proteins), *Neisseria meningitidis* (≤ 0.12 mg/L), *Salmonella*, *Shigella*, *Streptococcus agalactiae* (≤ 0.12-0.5 mg/L), *Streptococcus canis* (100% susceptible at 0.06 mg/L), *Streptococcus pneumoniae* (in Australia, 3% resistant), *Streptococcus pyogenes*

(≤ 0.12 mg/L); *Staphylococcus aureus* 85% acquired resistance due to β-lactamase; *Klebsiella* 98% intrinsic resistance due to β-lactamase (probably all resistant in clinical practice); *Enterobacter*, *Serratia, Citrobacter freundii*, *Proteus vulgaris*, *Providencia* 96% intrinsic resistance (probably all resistant in clinical practice), *Moraxella catarrhalis* 94% acquired resistance due to β-lactamase (possibly all resistant in clinical practice); *Pseudomonas aeruginosa* 100% intrinsic resistance; *Stenotrophomonas maltophilia* 100% intrinsic resistance; *Bacteroides fragilis* 100% intrinsic resistance due to β-lactamase; in Australia, *Escherichia coli* 48% resistance due to β-lactamase, *Proteus mirabilis* 18% resistance due to β-lactamase; significant inoculum effect; mode of elimination renal; incompatible with erythromycin, gentamicin, kanamycin, lincomycin, polymyxin B, tetracycline; oral ampicillin largely replaced by oral amoxycillin; in WHO Model List of Essential Drugs

Indications: amnionitis; septic arthritis due to *Listeria monocytogenes;* bacteremia and septicemia (infection from female genital tract, focus probably biliary or gastrointestinal tract, focus probably urinary tract, neonatal, due to *Salmonella*, *Shigella*, *Oerskovia*, *Enterococcus*); brain abscess from ear and mastoid or due to *Listeria monocytogenes* or *Haemophilus*; bronchectasis; bronchitis; acute chest infections; cholangitis and cholecystitis in normal host; infantile diarrhoea; bacterial dysentery; disseminated gonococcal and meningococcal disease; endocarditis treatment and prophylaxis; enteric fever treatment and carriers; acute epididymitis and epididymoorchitis; acute epiglottitis in normal host; simple gastritis, duodenal ulcer, peptic ulcer; bacterial gastroenteritis; purulent conjunctivitis due to *Listeria monocytogenes*; severe uncomplicated gonorrhoea; hepatitis due to *Shigella*; hepatic abscess; hepatic granuloma due to *Listeria monocytogenes*; mild leptospirosis; listeriosis; Lyme disease (arthritis, Bell's palsy, mild cardiac disease); lymph gland infections due to *Brucella*; neonatal and post-neonatal pyogenic meningitis due to *Listeria monocytogenes*, *Pasteurella multocida*); listerial meningoencephalitis; myocarditis and pericarditis due to *Actinomyces*, *Haemophilus influenzae*, *Listeria monocytogenes*; nasopharyngitis; osteomyelitis and osteochondritis due to *Listeria monocytogenes*, *Eikenella corrodens*; treatment and prophylaxis of otitis media; pancreatic abscess; peritonitis (suspected bowel origin, spontaneous, due to *Capnocytophaga*, *Listeria monocytogenes*); peritonsillar abscess in normal host; pertussis; pneumonia (moderate community acquired, severe *Haemophilus influenzae*); post-partum infections; severe acute prostatitis and seminal vesiculitis; prosthetic implants prophylaxis; severe acute pyelonephritis; rape prophylaxis; local and generalised sepsis (including due to *Enterococcus*, *Salmonella*); acute maxillary sinusitis; splenic abscess due to *Listeria monocytogenes*; surgical prophylaxis (ruptured, perforated or gangrenous viscus; postsplenectomy; joint); systemic infection prophylaxis in agammaglobulinemia; acute tracheitis; typhoid carriers; non-gonococcal urethritis; urinary tract infections; streptococcal vaginitis

Side Effects: sensitivity reactions to penicillin, anaphylactic shock in hypersensitive patients; skin reactions (especially in glandular fever; increased incidence of rash when combined with allopurinol), nausea, vomiting, diarrhoea, enterocolitis, pseudomembranous colitis, superinfection, hearing loss; safe in therapeutic amounts during pregnancy; modify dosage interval in renal dysfunction (rarely, seizures, interstitial nephritis, sodium overload, hypokalemia) and in dialysis; probenecid increases levels; weak association with oral contraceptive failure; unpredictable enhanced warfarin effect; safety in pregnancy not established; safe in breastfeeding but monitor infant for diarrhoea

Contraindications: penicillin hypersensitivity

AMOXYCILLIN (AMOXICILLIN): moderate spectrum, β-lactamase sensitive aminopenicillin; oral dosage schedule 3 times daily; more readily absorbed after oral administration than ampicillin (not affected by food) but parenterally equivalent; mean peak serum concentration 7.7 mg/L after 0.8 mole oral dose; 66% urinary recovery; 3.5% bronchial penetration 2-3 h after 1 g oral dose; intraperitoneal penetration 84%; protein binding 15%; mode of elimination renal; moderate cost; greater activity than benzylpenicillin against some Gram negative organisms; agent of choice against *Enterococcus*; oral amoxycillin preferred to oral ampicillin except in treatment of shigellosis; in WHO Model List of Essential Drugs

Indications: as for ampicillin; also purulent conjunctivitis due to *Neisseria* in remote areas; acute otitis media in remote areas; meningitis due to *Haemophilus influenzae* and *Listeria monocytogenes*; mild to moderate community acquired pneumonia in adult > 60 y or with coexisting illness and in child 3 mo - 10 y; acute sinusitis; gonorrhoeal vaginitis (β-lactamase negative)

Side Effects: low risk of serious adverse reactions and skin rash (increased risk of rash in patients receiving allopurinol); moderate risk of gastrointestinal adverse effects; pseudomembranous colitis; allergic reactions; adjustment of dosage interval in renal failure (rarely, seizures) and in dialysis; safe in pregnancy; probenecid increases plasma levels; weak association with oral contraceptive failure; unpredictable enhanced warfarin effect

AMDINOCILLIN PIVOXIL: moderate spectrum penicillin; binds chiefly to PBP2; kills only growing organisms; not affected by type I β-lacamase; low inducer of type I β-lactamase; spectrum includes *Escherichia coli* (MIC 0.13 mg/L)

Indications: bacterial dysentery

APALCILLIN: moderate spectrum penicillin; spectrum includes β-lactamase negative *Haemophilus influenzae* (MIC ≤ 0.5 mg/L), β-lactamase negative *Neisseria gonorrhoeae* (≤ 0.5 mg/L), *Neisseria meningitidis* (0.5 mg/L), *Proteus mirabilis* (≤ 0.5 mg/L), *Streptococcus agalactiae* (≤ 0.5 mg/L), *Streptococcus pneumoniae* (≤ 0.02-1 mg/L), *Streptococcus pyogenes* (≤ 0.02-0.5 mg/L)

BACAMPICILLIN: moderate spectrum penicillin; mean peak serum concentration 8.2 mg/L after 0.8 mole oral dose; 55% urinary recovery

FORAMINDOCILLIN: moderate spectrum penicillin; spectrum includes *Escherichia coli* (0.12-0.5 mg/L), *Haemophilus influenzae* (0.06-0.12 mg/L), *Klebsiella oxytoca* (0.25-0.5 mg/L), *Klebsiella pneumoniae* (0.25-0.5 mg/L), *Proteus mirabilis* (0.25-0.5 mg/L)

HETACILLIN: moderate spectrum penicillin; activity equal to ampicillin

Side Effects: safety not established in pregnancy

MECILLINAM: moderate spectrum penicillin; serum protein binding 5%; spectrum includes Group IIf (MIC 0.5-1 mg/L)

PIVAMPICILLIN: moderate spectrum penicillin; mean peak serum concentration 7.1 mg/L after 0.8 mole oral dose; 70% urinary recovery

Indications: bacterial gastroenteritis

PIVEMECILLINAM

Indications: bacterial gastroenteritis

TALAMPICILLIN: moderate spectrum penicillin; mean peak serum concentration 5.3 mg/L after 0.8 mole oral dose; 75% urinary recovery; intraperitoneal penetration 48%; protein binding 85%

TEMOCILLIN: moderate spectrum penicillin; spectrum includes *Haemophilus influenzae* (MIC 0.25-0.5 mg/L), *Neisseria gonorrhoeae* (0.5-1 mg/L), *Neisseria meningitidis* (0.12 mg/L)

CARBENICILLIN: extended spectrum (broad spectrum and *Pseudomonas aeruginosa*), very acid stable penicillin; orally ineffective; implicated in emergence of multiple drug resistance during therapy; less active than ampicillin against *Neisseria meningitidis*, non-β-lactamase-producing *Staphylococcus aureus* and streptococci; more active than ampicillin against *Proteus*; spectrum includes *Actinomyces* (100% susceptible), anaerobic cocci (100% susceptible), *Arachnia* (100% susceptible), *Clostridium* (100% susceptible), *Erysipelothrix* (100% susceptible), β-lactamase negative *Haemophilus influenzae* (0.5 mg/L), *Hafnia alvei* (100% susceptible), *Moraxella* (≤ 0.06-0.25 mg/L), *Neisseria meningitidis* (0.5 mg/L), *Proteus mirabilis* (1 mg/L), *Streptococcus pneumoniae* (0.25 mg/L), *Streptococcus pyogenes* (0.25-1 mg/L); no inoculum effect with aerobes, shows inoculum effect with anaerobes; incompatible with chloramphenicol, erythromycin, gentamicin, lincomycin, streptomycin, tetracycline

Indications: anaerobic cellulitis, endocarditis, meningitis, otitis externa, pneumonia, septicemia, urinary tract infection; replaced by ticarcillin

Side Effects: pain at injection site, platelet dysfunction, sodium overload; leucopoenia, eosinophilia, drug fever and rash with total dose > 750 g; safety not established during pregnancy; modify dosage in renal dysfunction (platelet inhibition); further dose required after hemodialysis

TICARCILLIN: broad spectrum and antipseudomonal (high doses required); serum protein binding 40%; no postantibiotic effect; implicated in emergence of multiple drug resistance during therapy; no inoculum effect; mode of elimination renal; more expensive than most other penicillins; spectrum includes *Actinomyces* (100% susceptible), *Alcaligenes denitificans* (MIC 0.5-1 mg/L), anaerobic cocci (100% susceptible), *Arachnia* (100% susceptible), *Clostridium* (100% susceptible), β-lactamase negative *Haemophilus influenzae* (0.5 mg/L), β-lactamase negative *Neisseria gonorrhoeae* (0.5-1 mg/L), *Neisseria meningitidis* (0.5 mg/L), *Peptostreptococcus asaccharolyticus* (≤ 1 mg/L), *Peptostreptococcus prevoti* (≤ 1 mg/L), *Propionibacterium acnes* (≤ 1mg/L), *Streptococcus pneumoniae* (0.25-1 mg/L), *Streptococcus pyogenes* (0.25-1 mg/L); *Staphylococcus aureus* 85% acquired resistance due to β-lacamase, *Klebsiellla* 98% intrinsic resistance due to β-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 48% resistant due to β-lactamase, *Proteus mirabilis* 18% resistant due to β-lactamase, *Pseudomonas aeruginosa* 13% resistant

Indications: septic arthritis due to *Pseudomonas aeruginosa* in immunocompromised; cellulitis due to aerobic Gram negatives; purulent conjunctivitis due to *Pseudomonas aeruginosa;* endocarditis due to Gram negative bacilli; otitis externa; nosocomial otitis media; *Pseudomonas aeruginosa* infections; rhabdomyolysis

Side Effects: modify dose in renal dysfunction (platelet inhibition; rarely, seizures, interstitial nephritis, sodium overload, hypokalemia); further dose required after haemodialysis; probably safe in pregnancy

PIPERACILLIN: broad spectrum and antipseudomonal (high doses required) ureidopenicillin; binds chiefly to PBP3; kills only growing organisms; more active against enterococci than ticarcillin; spectrum includes *Actinomyces* (100% susceptible), *Aeromonas hydrophila* (100% susceptible), *Alcaligenes denitrificans* (MIC 0.25-1 mg/L), anaerobic cocci (100% susceptible at < 1 mg/L), *Arachnia* (100% susceptible), *Bordetella bronchiseptica* (0.5-1 mg/L), *Clostridium* (100% susceptible), Group IIf (≤ 0.06 mg/L), *Hafnia alvei* (100% susceptible), *Moraxella catarrhalis* (< 0.015-1 mg/L), penicillinase negative *Neisseria gonorrhoeae* (0.06 mg/L), *Neisseria meningitidis* (≤ 0.5 mg/L), *Streptococcus agalactiae* (≤ 0.5 mg/L), *Streptococcus pneumoniae* (1 mg/L), *Streptococcus pyogenes* (≤ 0.02-0.15 mg/L), *Streptococcus viridans* (0.5 mg/L); *Staphylococcus aureus* 85% acquired resistance due to β-lactamase, *Klebsiellla* 98% intrinsic resistance due to β-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 48% resistance due to β-lactamase, *Proteus mirabilis* 18% resistance due to β-lactamase, *Pseudomonas aeruginosa* 9% resistance; implicated in emergence of multiple drug resistance during therapy; may show inoculum effect; in WHO Model List of Essential Drugs; more expensive than most other penicillins

Indications: bacteremia and septicemia (due to *Burkholeria pseudomallei*, *Pseudomonas aeruginosa*, *Yersinia enterocolitica*, *Campylobacter fetus subsp fetus, Methylobacterium extorquens, Agrobacterium tumefaciens);* cervical fascial space infections

in immunocompromised; purulent conjunctivitis due to *Pseudomonas aeruginosa;* malignant otitis externa due to *Pseudomonas aeruginosa;* perianal and perirectal abscess in patients with malignant disease; peritonsillar abscess in immunocompromised; endomyometritis and endometritis; febrile neutropenic patients

Side Effects: leucopenia, drug fever, thrombocytopenia, eosinophilia, urticarial rash, pruritis, hepatic damage; rare reports of hemolytic anemia in patients with CSF; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; dose interval adjustment required in renal failure and in dialysis; increased duration of neuromuscular blockade with vecuronium; reduces methotrexate clearance with possible increase in toxicity

AZLOCILLIN: broad spectrum and antipseudomonal ureidopenicillin; more active than ticarcillin against *Pseudomonas* in vitro; spectrum includes *Alcaligenes denitrificans* (MIC 0.13-0.25 mg/L), *Bordetella bronchiseptica* (0.5-1 mg/L), *Moraxella* (≤ 0.06-0.5 mg/L), *Neisseria meningitidis* (≤ 0.5 mg/L), *Proteus mirabilis* (< 1 mg/L), *Streptococcus agalactiae* (≤ 0.5 mg/L), *Streptococcus canis* (100% susceptible at 0.125 mg/L), *Streptococcus pneumonia* (≤ 0.02-1 mg/L), *Streptococcus pyogenes* (≤ 0.02-0.5 mg/L); *Staphylococcus aureus* 90% acquired resistance due to β-lactamase, *Klebsiella* 98% intrinsic resistance due to β-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 45% resistant due to β-lactamase, 14% *Proteus mirabilis* resistant due to β-lactamase; reduced clearance in elderly; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect

Indications: bacteremia and septicemia due to *Pseudomonas aeruginosa*; endocarditis due to *Pseudomonas aeruginosa*; neonatal and postneonatal pyogenic meningitis due to *Pseudomonas aeruginosa*; myocarditis and pericarditis due to *Pseudomonas aeruginosa*

Side Effects: leucopenia, drug fever, thrombocytopenia, eosinophilia, rash, hepatic damage; dose adjustment needed in renal failure and dialysis

MEZLOCILLIN: broad spectrum and antipseudomonal ureidopenicillin; binds chiefly to PBP3; roughly equivalent to ticarcillin in vitro; spectrum includes *Actinomyces* (100% susceptible), *Aeromonas hydrophila* (100% susceptible), anaerobic cocci (100% susceptible), *Arachnia* (100% susceptible), *Clostridium* (100% susceptible), β-lactamase negative *Haemophilus influenzae* (≤ 0.5 mg/L), *Hafnia alvei* (100% susceptible), β-lactamase negative *Neisseria gonorrhoeae* (0.08 mg/L), *Neisseria meningitidis* (≤ 0.5 mg/L), *Proteus mirabilis* (≤ 1 mg/L), *Streptococcus agalactiae* (≤ 0.5 mg/L), *Streptococcus canis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (< 0.02 mg/L), *Streptococcus pyogenes* (≤ 0.02-0.5 mg/L); implicated in emergence of multiple drug resistance during therapy; shows inoculum effect

Indications: large bowel surgical prophylaxis

Side Effects: leucopenia, drug fever, thrombocytopenia, eosinophilia, rash, hepatic damage

CLAVULANIC ACID: Class 2 β-lactamase inhibitor; used in combination with amoxycillin to treat β-lactamase-producing *Neisseria gonorrhoeae* and *Haemophilus influenzae*; also inhibits β-lactamases produced by *Escherichia coli*, *Klebsiella*, *Proteus mirabilis*, *Proteus vulgaris*, *Moraxella catarrhalis*, *Bacteroides*, *Staphylococcus aureus*; combination with ticarcillin also available; binds chiefly to PBP2; serum protein binding 20%

AMOXYCILLIN-CLAVULANATE (AUGMENTIN): broad spectrum; expensive; oral dose schedule 3 times daily; take immediately before or with first mouthful of food; spectrum includes anaerobes (100% susceptible), *Campylobacter fetus* (0.25-1 mg/L), *Capnocytophaga canimorsus* (95% susceptible), *Eikenella corrodens* (100% susceptible), *Enterococcus* (100% susceptible), *Haemophilus influenzae* (< 5% resistance in Australia), *Listeria monocytogenes* (100% susceptible at 0.25 mg/L), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), *Neisseria meningitidis* (100% susceptible at 0.12 mg/L), *Pasteurella multocida* (100% susceptible), *Pseudomonas stutzeri* (100% susceptible), *Shigella* (100% susceptible), methicillin susceptible *Staphylococcus aureus* (100% susceptible at 1 mg/L), *Staphylococcus intermedius* (100% susceptible), *Streptococcus agalactiae* (100% susceptible at 0.12 mg/L), *Streptococcus equinus* (100% susceptible at 0.12 mg/L), *Streptococcus pneumoniae* (100% susceptible at 1 mg/L), *Streptococcus pyogenes* (100% susceptible at ≤ 0.06 mg/L); *Enterobacter*, *Citrobacter freundii*, *Proteus vulgaris*, *Providencia*, *Serratia* 92% intrinsic resistance due to β-lactamase (possibly all resistant in clinical practice); *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* 100% intrinsic resistance; in Australia, *Escherichia coli* 27% resistance due to β-lactamase, *Klebsiella pneumoniae* 11% resistant, *Proteus mirabilis* 9% resistant due to β-lactamase; in WHO Model List of Essential Drugs; more expensive than amoxycillin

Indications: should be reserved for treatment of organisms in which resistance to amoxycillin is due to enzyme which clavulanic acid can inhibit; abortional and puerperal infections; septic arthritis (unknown organism in < 5 years old) *Haemophilus influenzae*, *Eikenella corrodens*; bacteremia and septicemia due to *Burkholderia pseudomallei*, *Yersinia enterocolitica*, *Campylobacter fetus* subsp *fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens*; bronchitis; cat, dog and human bite and clenched fist injury infections; less severe cellulitis due to *Haemophilus influenzae*; chancroid; cholecystitis; chorioamnionitis; acute cystitis in adults; diverticulitis; acute epididymitis and epididymoorchitis; epiglottitis in normal host; chronic mastitis and breast abscess; postneonatal pyogenic meningitis due to *Moraxella catarrhalis*; osteomyelitis and osteochondritis due to *Staphylococcus aureus*; otitis media; parotitis and submandibular sialadenitis due to *Burkholderia pseudomallei;* pneumonia (resistant organism or slow response in mild to moderate community acquired in adult > 60 y or with coexisting illness or in child 3 mo -10 y, mild *Haemophilus influenzae*, *Moraxella catarrhalis*, mild anaerobic, mild

nosocomial with no specific risk factors); *Haemophilus influenzae* pneumonitis; postpartum fever and endometritis; preseptal cellulitis in < 4 y old; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; mild acute pyelonephritis; acute maxillary sinusitis; tooth abscess unresponsive to treatment; acute tracheitis; less severe ulcers in diabetics; *Haemophilus* and other non-gonococcal urethritis; suppurative wound infections

Side Effects: low risk of serious adverse reactions and skin rash; very high risk of gastrointestinal adverse effects (diarrhoea more frequent than with amoxycillin); hepatotoxicity more frequent than with amoxycillin; can cause cholestasis; probably safe in pregnancy; dose adjustment required in renal failure and in dialysis; unpredictable enhanced warfarin effect

Contraindications: avoid in breastfeeding (insufficient data; monitor infant for diarrhoea)

TICARCILLIN-CLAVULANATE (TIMENTIN): broad spectrum and antipseudomonal; parenteral; spectrum includes *Actinomyces* (100% susceptible), *Bacteroides* (99-100% susceptible at 128 mg/L), *Clostridium* (100% susceptible), *Fusobacterium* (97% susceptible), *Peptostreptococcus* (100% susceptible), *Propionibacterium acnes* (MIC $\leq$ 1 mg/L), *Proteus mirabilis* (100%), *Stenotrophomonas maltophilia* (98% of hospital isolates); more expensive than most other penicillins

Indications: should be reserved for treatment of organisms in which resistance to ticarcillin is due to enzyme which clavulanic acid can inhibit; bacteremia and septicemia (focus probably decubitus or ischemic ulcer or diabetic foot ulcer, febrile neutropenic patients without renal impairment/not on nephrotoxic drugs, *Pseudomonas aeruginosa* suspected); severe bite and clenched fist injuries; hepatic abscess; treatment and prophylaxis of mixed aerobic and anaerobic infections; pancreatic abscess; parametritis and pelvic inflammatory disease due to coliforms; peritonitis of suspected bowel origin; pneumonia (mild to moderate community acquired with risk factors, severe nosocomial); surgical prophylaxis (total hip replacement); severe ulcers in diabetics

Side Effects: dose adjustment required in renal failure and dialysis; safety in pregnancy and breastfeeding not established (monitor infant for diarrhoea if breastfeeding)

SULBACTAM: β-lactamase inhibitor (same range of organisms as clavulanic acid); intraperitoneal penetration 92%; protein binding $\approx$ 20%; low inducer of type I β-lactamase

Indications: multiresistant *Acinetobacter baumannii* infections

AMPICILLIN-SULBACTAM: i.v.

Indications: chronic mastitis and breast abscess (organisms in which resistance to ampicillin is due to enzyme which sulbactam can inhibit); mixed Gram positive and anaerobic infections such as community acquired aspiration pneumonia, diabetic foot infections, decubitus infections, mild to moderate intraabdominal infections; i.v. drug of choice for empiric treatment of animal bites; prophylaxis for colorectal surgery; *Acinetobacter baumannii* bacteraemia

TAZOBACTAM: β-lactamase inhibitor (same range of organisms as clavulanic acid); apparently less likely than clavulanic acid or sulbactam to induce production of β-lactamases leading to failure of therapy of *Citrobacter, Enterobacter, Pseudomonas, Serratia*

PIPERACILLIN-TAZOBACTAM: broad spectrum and antipseudomonal; spectrum includes *Escherichia coli* (97% of hospital isolates), *Klebsiella oxytoca* (93% of hospital isolates), *Klebsiella pneumoniae* (96% of hospital isolates), *Proteus mirabilis* (100%), *Pseudomonas aeruginosa* (91% of hospital isolates); greater in vitro activity against enterococci and *Klebsiella* than ticarcillin-clavulanate but more expensive

Indications: similar to timentin; bacteremia, septicemia and septic shock (unidentified source in febrile neutropenic patients with no renal impairment and not on nephrotoxic drugs and with *Pseudomonas aeruginosa* suspected); nosocomial mixed aerobic/anaerobic infections, including pelvic and abdominal infections and pneumonia; empirical therapy in febrile neutropenic patient; treatment of ischemic/diabetic foot

Side Effects: those of piperacillin; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; requires dosage interval adjustment in renal failure and in dialysis

Contraindications: avoid if breastfeeding (insufficient data)

CARBAPENEMS: very broad spectrum of potent antibacterial activity; postantibiotic effect; inactivated by metallo-β-lactamases; produce relatively low amounts of endotoxins; used in mixed infections and neutropenic patients; widespread use has been linked with increasing prevalence of infections due to methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, multi-resistant Gram-negative organisms and *Clostridium difficile*; expensive and regarded as reserve agents

Side Effects: thrombophlebitis at injection site, nausea, diarrhoea, vomiting common; fever, rash, itch, paraesthesia, headache, dizziness, somnolence, confusion, tremor, encephalopathy, psychiatric disturbances, seizures, blood dyscrasias uncommon; pseudomembranous colitis, hepatitis, anaphylaxis, erythema multiforme, angioedema, Stevens-Johnson syndrome, tachycardia, renal toxicity rare; dose adjustment required in renal impairment

THIENAMYCIN: structure similar to clavulanic acid but has broad antibacterial activity (Enterobacteriaceae and *Pseudomonas* comparable to aminoglycosides, excellent activity against anaerobes including *Bacteroides fragilis* and most Gram positive cocci) as well as possessing potent β-lactamase inhibition; spectrum includes *Bacteroides fragilis* (100% susceptible), *Enterococcus faecalis* (MIC 1 mg/L), *Escherichia coli* (0.25 mg/L), *Staphylococcus aureus* ($\leq$ 0.06 mg/L)

IMIPENEM: N-formimidoyl thienamycin; greater stability than thienamycin; kills non-growing organisms; inactivated by renal dipeptidase and therefore combined with dipeptidase inhibitor cilastatin; may show inoculum effect; activity against Gram negative bacilli and *Pseudomonas aeruginosa* equivalent to that of aminoglycosides, excellent activity against anaerobes and many Gram positive organisms; not active against methicillin resistant *Staphylococcus aureus, Enterococcus faecium, Stenotrophomonas, Mycoplasma, Chlamydia* and some species of *Pseudomonas*; relatively expensive; broadest spectrum of any β-lactam available; spectrum includes *Achromobacter* (100% susceptible), *Acinetobacter* (98% of hospital isolates), *Actinomyces* (100% susceptible), *Aeromonas*, *Alcaligenes* (100% susceptible), *Parabacteroides distasonis* (99% susceptible), *Bacteroides fragilis* (100% susceptible at 8 mg/L), *Campylobacter gracilis* (100% susceptible at 8 mg/L), *Bacteroides thetaiotaomicron* (99% susceptible), *Bordetella bronchiseptica* (100% susceptible), *Campylobacter* (100% susceptible), *Citrobacter* (100%), *Clostridium* (99-100% susceptible at < 1 mg/L), *Enterobacter aerogenes* (94% of hospital isolates), *Enterobacter cloacae* (100%), Enterobacteriaceae (< 5% resistance in Australia), *Escherichia coli* (0.1% resistant in Australia), *Eubacterium* (100% susceptible), *Fusobacterium* (90-95% susceptible at < 1 mg/L), *Gardnerella vaginalis* (100% susceptible), *Haemophilus influenzae* (0.5 mg/L), *Klebsiella oxytoca* (100% susceptible at < 1 mg/L), *Klebsiella pneumoniae* (0.4% resistant in Australia), *Legionella* (≤ 0.004-1 mg/L), *Listeria monocytogenes* (100% susceptible at < 1 mg/L), *Moraxella* (96% susceptible), *Morganella morganii* (100% susceptible), *Neisseria* (100% susceptible at < 1 mg/L), *Nocardia* (98% susceptible at < 1 mg/L), *Peptococcus* (100% susceptible at < 1 mg/L), *Peptostreptococcus* (100% susceptible at < 1 mg/L), *Prevotella melaninogenica* (99% susceptible), *Propionibacterium* (100% susceptible), *Proteus mirabilis* (18% resistant in Australia), *Proteus vulgaris* (100%), *Providencia stuartii* (100% susceptible), *Salmonella* (100% susceptible at < 1 mg/L), *Serratia liquefaciens* (100% susceptible), *Serratia marcescens* (100%), *Shigella* (100% susceptible at < 1 mg/L), methicillin susceptible *Staphylococcus aureus* (100% susceptible at < 1 mg/L), *Streptococcus agalactiae* (100% susceptible), *Streptococcus canis* (100% susceptible), *Streptococcus* group C (100% susceptible), *Streptococcus pneumoniae* (100% susceptible at < 1 mg/L), *Streptococcus pyogenes* (100% susceptible at < 1 mg/L), *Streptococcus viridans* (100% susceptible), *Veillonella* (100% susceptible), *Wolinella* (≤ 1 mg/L), *Yersinia* (100% susceptible); *Stenotrophomonas maltophilia* 100% intrinsic resistance due to β-lactamase; methicillin resistant *Staphylococcus aureus*, *Enterococcus faecium*, some strains of *Burkholderia cepacia* and *Pseudomonas* (in Australia, 17% of *Pseudomonas aeruginosa*) resistant; expensive; in WHO Model List of Essential Drugs

Indications: restricted at present to complicated nosocomial infections and infections due to multiply resistant Gram negative bacilli; bacteremia and septicemia (febrile neutropenic patients with renal impairment/on nephrotoxic drugs, neutrophil count 500-1000/μL, due to *Acinetobacter*, *Burkholderia pseudomallei*); bone and joint infections; cervical fascial space infection in immunocompromised; cervical parameningeal deep fascial space infections in immunocompromised; emphysematous gastritis; endocarditis due to *Acinetobacter*, *Alcaligenes*; gynaecological infections; intraabdominal infections; severe nosocomial pneumonia; postneonatal meningitis due to *Nocardia asteroides*, *Acinetobacter*; polymicrobial infections; skin and soft structure infections

Side Effects: CNS toxicity (seizures in 1%; increased risk with ganciclovir) in renal insufficiency (adjust dose appropriately and avoid daily dose of > 2 g), nausea and vomiting in 2%; dose adjustment required in dialysis; avoid cilastatin if glomerular filtration rate < 10 mL/min and in dialysis; safety in pregnancy not established; safe in breastfeeding

MEROPENEM: carbapenem resistant to renal dipeptidase; attains better levels in CSF than imipenem; spectrum includes *Aeromonas* (MIC ≤ 0.06-1 mg/L), *Bacteroides* (0.13-0.5 mg/L), *Bifidobacterium* (1 mg/L), *Burkholderia cepacia* (best MIC_{90}), *Citrobacter* (≤ 0.06-0.13 mg/L), *Clostridium* (≤ 0.06-4 mg/L), *Enterobacter* (0.13-0.25 mg/L), *Escherichia coli* (≤ 0.06 mg/L), *Eubacterium* (0.03-0.13 mg/L), *Hafnia alvei* (0.06 mg/L), *Klebsiella* (0.03-0.25 mg/L), *Morganella morganii* (0.25 mg/L), *Pasteurella multocida* (0.13 mg/L), *Peptococcus* (0.03-0.25 mg/L), *Peptostreptococcus* (0.13-2 mg/L), *Plesiomonas shigelloides* (≤ 0.06 mg/L), *Propionibacterium* (0.25 mg/L), *Proteus* (0.13-0.5 mg/L), *Providencia* (0.13-0.5 mg/L), *Pseudomonas* (0.25-8 mg/L), *Salmonella* (≤ 0.06 mg/L), *Serratia* (0.13- 0.25 mg/L), *Shigella* (0.03-0.06 mg/L), methicillin susceptible *Staphylococcus* (0.25-4 mg/L), *Streptococcus* (≤ 0.01-8 mg/L), *Yersinia enterocoliticia* (0.06 mg/L); *Stenotrophomonas maltophilia* 100% intrinsic resistance; expensive

Indications: could find place in therapy of seriously ill hospital patients, especially those with intra-abdominal infections, neutropenic cancer patients and intensive care unit patients with lower respiratory tract infections and hospital acquired meningitis

Side Effects: rare seizures (lower incidence than imipenem), nausea and vomiting in 1%; safety in pregnancy not established; caution in breastfeeding (monitor infant for diarrhoea)

ERTAPENEM: once a day injectable carbapenem; active against anaerobes, Gram positive and Gram negative aerobic bacteria and is resistant to some β-lactamases but does not cover *Acinetobacter, Pseudomonas,* penicillin resistant *Streptococcus pneumoniae,* β-lactamase positive *Haemophilus influenzae*

Indications: moderate to severe adult bacterial infections caused by gram positive and gram negative aerobic and anaerobic bacteria suspected or proven resistant to all other antibiotics or in patients unable to tolerate other antibiotics; initial empiric therapy of complicated intra-abdominal infections and acute pelvic infections including post-partum endomyometritis, septic abortion and post-surgical gynaecological infections

Side Effects: diarrhoea, infused vein complications, nausea, headache, vaginitis, vein inflammation, vomiting

CEPHALOSPORINS: inhibit transpeptidase thus preventing cross-linking of cell wall peptidoglycan; bactericidal; act only on proliferating bacteria; in high concentrations, penetrate into mammalian cells; active against Gram positive and Gram negative bacteria; spectrum includes *Actinomyces*, *Cardiobacterium hominis, Corynebacterium diphtheriae; Enterococcus* 100% intrinsic resistance, *Pseudomonas aeruginosa* 100% intrinsic resistance (except ceftazidime, cefepime, cefpirome), *Stenotrophomonas maltophilia* 100% intrinsic resistance (except ceftazidime), *Bacteroides fragilis* 100% intrinsic resistance (except cefoxitin and cefotetan); widespread use linked to increased prevalence of methicillin resistant staphylococci, vancomycin resistant enterococci, drug-resistant *Streptococcus pneumoniae,* multiresistant Gram negative organisms, and *Clostridium difficile*; no effect on opsonisation, decrease neutrophil chemotaxis, no effect on phagocytosis, no effect on bacterial adherence, increase capsule enzyme/toxin, decrease intracellular killing

Indications: intraabdominal infections; ischiorectal abscess; otitis externa due to *Corynebacterium diphtheriae*, *Actinomyces israelii*; post-surgery peritonitis; localised staphylococcal skin lesions; surgical prophylaxis (total hip replacement); systemic infection in agammaglobulinemia, C1, 2, 3, 4, factor B deficiency, hyposplenism/splenectomy; tetanus

Side Effects: diarrhoea, nausea, rash, eosinophilia, drug fever, electrolyte disturbances, pain and inflammation at injection site, pseudomembranous colitis common; vomiting, headache, dizziness, oral and vaginal candidiasis uncommon; hypersensitivity reactions including anaphylactic shock (cross-hypersensitivity can occur in 3-6% of penicillin allergic subjects), interstitial nephritis, neurotoxicity, blood dyscrasias, bleeding, renal impairment, bone marrow suppression, hemolysis, megaloblastic marrow, superinfection, aseptic meningitis rare; probably all safe in therapeutic amounts during pregnancy; modify dose in renal failure (CNS toxicity); require further dose after hemodialysis; maximum permissible blood level 32 mg/L; probenecid increases plasma levels

CEPHALOTHIN: moderate spectrum parenteral first generation cephalosporin active against β-lactamase-producing staphylococci (highly susceptible) and some Enterobacteriaceae; streptococci highly susceptible but not active against *Enterococcus faecalis*; poor activity against *Haemophilus influenzae*, *Bacteroides fragilis*, *Serratia*, *Enterobacter*, *Pseudomonas*; not active against *Listeria monocytogenes;* spectrum includes *Erysipelothrix* (100% susceptible at ≤ 1 mg/L), *Helicobacter pylori*, *Neisseria meningitidis* (< 5% resistance in Australia), methicillin susceptible *Staphylococcus aureus* (MIC 0.06-0.5 mg/L), *Streptococcus pneumoniae* (0.25 mg/L), *Streptococcus pyogenes* (0.12 mg/L); *Enterobacter, Serratia, Citrobacter freundii, Proteus vulgaris, Providencia* 92% intrinsic resistance due to β-lactamase (probably all resistant in clinical practice); in Australia, *Escherichia coli* 32% resistant due to β-lactamase, *Klebsiella pneumoniae* 21% resistant due to β-lactamase, *Proteus mirabilis* 10% resistant due to β-lactamase; poorly absorbed; strongly hydrolysed by type I β-lactamase; moderate inducer of type I β-lactamase; serum levels increased and prolonged by probenecid; increased V_d, reduced clearance in elderly; minimal inoculum effect; CSF penetration 0 - > 50%; mode of elimination renal; incompatible with colistimethate, erythromycin, gentamicin, kanamycin, lincomycin, tetracycline

Indications: one of most important agents for prophylaxis in orthopedic and vascular surgery where prostheses are being inserted; staphylococcal septic arthritis in penicillin hypersensitive patients; bacteremia and septicemia (infection from female genital tract in penicillin hypersensitive, focus probably biliary or gastrointestinal in penicillin hypersensitive, focus probably open skin infection/cellulitis, focus decubitus or ischemia or diabetic foot ulcer in penicillin hypersensitive, due to *Staphylococcus aureus*, due to *Streptococcus pyogenes* in penicillin hypersensitive, unidentified source); severe streptococcal and staphylococcal cellulitis in penicillin hypersensitive; compound fractures; severe erysipelas in penicillin hypersensitive; local and generalised sepsis (organism not known); osteomyelitis and osteochondritis due to *Staphylococcus aureus* in penicillin hypersensitive; pneumonia (Gram negative, staphylococcal, mild to moderate community acquired in adult); severe acute pyelonephritis; septicemia; surgical prophylaxis (cardiovascular; vascular graft; breast; dialysis access; orthopedic; head, neck and thoracic; gastrointestinal; colorectal; appendectomy; hysterectomy; termination of pregnancy; renal transplantation; liver transplantation; muscular, skeletal and soft tissue trauma; endoscopic procedures; caesarean section); staphylococcal toxic shock syndrome; severe ulcers in diabetics

Side Effects: positive direct Coomb's test (uncommonly, associated hemolytic anemia with very large doses), pain and local reaction at injection site; hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome; dose adjustment required in renal failure and in dialysis; avoid use in severe renal dysfunction (nephrotoxicity (interstitial nephritis), enhanced by aminoglycosides and large doses of ethacrynic acid or frusemide, particularly in elderly; may falsely elevate serum creatinine measurement by certain assays; rarely, seizures); safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

CEPHAPIRIN: parenteral first generation cephalosporin; minimal to significant inoculum effect

Side Effects: hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome

CEPHRADINE: first generation cephalosporin; can be given parenterally or orally; 15% bronchial penetration after 1 g oral dose; serum levels increased and prolonged by probenecid; reduced clearance in elderly; withdrawn from market in mid 1980s

Side Effects: gastrointestinal disturbances, hypersensitivity syndrome, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome

CEPHALORIDINE: moderate spectrum parenteral first generation cephalosporin; poorly absorbed; less serum bound; binds chiefly to PBP1a; kills only growing organisms; serum levels not increased or prolonged by probenecid; activity equal to cephalothin; significant inoculum effect; no longer used because of nephrotoxicity

CEPHALEXIN: moderate spectrum first generation cephalosporin; well absorbed; can be given orally; not affected by food; similar activity to cephalothin; spectrum includes *Moraxella catarrhalis* (100% susceptible), β-lactamase negative *Neisseria gonorrhoeae* (100% susceptible), *Neisseria meningitidis* (100% susceptible), methicillin susceptible *Staphylococcus aureus* (100% susceptible), *Staphylococcus intermedius* (95% susceptible); *Enterobacter*, *Serratia*, *Citrobacter freundii*, *Proteus vulgaris*, *Providencia*, 92% intrinsic resistance due to β-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 7% resistant due to β-lactamase, *Klebsiella pneumoniae* 21% resistant due to β-lactamase, *Proteus mirabilis* 10% resistant due to β-lactamase; kills only growing organisms; serum levels increased and prolonged by probenecid; no significant change in absorption in elderly; mode of elimination renal (> 80%); half life 0.9 h; C_{max} 18 mg/L; bioavailability > 90%; inexpensive

Indications: has found important role in urinary and skin/soft tissue infections; excellent substitute for penicillin in some infections in hypersensitive patients; biliary infections; bullous impetigo; less severe streptococcal cellulitis in penicillin hypersensitive; diverticulitis; prophylaxis of recurrent nonvenereal dysuria-frequency syndrome; mild acute epididymitis and epididymoorchitis associated with urinary tract infection; less severe erysipelas in penicillin hypersensitive; severe impetigo; acute mastitis and breast abscess; aphthous mouth ulcers (compresses); nasal septal abscess; osteomyelitis and osteochondritis due to *Staphylococcus aureus;* pharyngitis; pneumonia; staphylococcal pyoderma treatment and prophylaxis; respiratory tract infections; staphylococcal local and generalised sepsis; acute sinusitis; less severe ulcers in diabetics; urinary tract infections (acute cystitis in adults, mild acute pyelonephritis); water-related infections in remote areas

Side Effects: hypersensitivity syndrome, fixed drug reaction, lupus erythematosus, pemphigus, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; vestibular ototoxicity and nephrotoxicity (interstitial nephritis) and, rarely, seizures in renal insufficiency (adjust dose appropriately); safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; dose interval adjustment required in dialysis; very weak association with oral contraceptive failure

CEFADROXIL: oral first generation cephalosporin

Side Effects: hypersensitivity syndrome, pemphigus, serum sickness-like illness, Stevens-Johnson syndrome, *Clostridium difficile*-associated diarrhoea

CEFPROZIL: oral first generation cephalosporin; *Staphylococcus aureus* and *Streptococcus pyogenes* highly susceptible, *Escherichia coli* and *Proteus mirabilis* susceptible, *Klebsiella* moderately susceptible, *Pseudomonas aeruginosa* resistant; half life 1.3 h; C_{max} 10.5 mg/L; bioavailability > 90%; renal excretion 61%

Indications: empirical use after amoxicillin/ampicillin failure in otitis media, sinusitis; completion of therapy with second generation cephalosporin

Side Effects: hypersensitivity syndrome, serum-sickness like illness, Stevens-Johnson syndrome

CEPHALOGLYCIN: moderate spectrum oral first generation cephalosporin; well absorbed; activity equal to cephalothin; no longer recommended

CEPHAZOLIN: parenteral first generation moderate spectrum cephalosporin; similar to cephalothin but more suitable for intramuscular use and longer half-life; spectrum includes *Streptococcus canis* (100% susceptible at 1 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L); *Enterobacter, Serratia, Citrobacter freundii, Proteus vulgaris, Providencia* 92% intrinsic resistance due to β-lactamase (possibly all resistant in clinical practice); in Australia, *Escherichia coli* 13% resistant due to β-lactamase, *Klebsiella pneumoniae* 21% resistant due to β-lactamase, *Proteus mirabilis* 10% resistant due to β-lactamase; reduced clearance in elderly; no to moderate postantibiotic effect; significant inoculum effect

Indications: septic arthritis due to *Staphylococcus aureus* in penicillin hypersensitive patient; bacteremia and septicemia (focus probably from skin/cellulitis, from female genital tract in penicillin hypersensitive, from decubitus or ischemic ulcer or diabetic foot ulcer in penicillin hypersensitive, unidentified source, methicillin sensitive *Staphylococcus aureus* in penicillin hypersensitive, *Streptococcus pyogenes* in penicillin hypersensitive); cellulitis due to *Streptococcus pyogenes* or *Staphylococcus aureus* in penicillin hypersensitive; cholangitis and cholecystitis; compound fractures; endocarditis; severe erysipelas in penicillin hypersensitive; local and generalised sepsis (organism not known); osteomyelitis; pneumonia (mild to moderate community acquired); surgical prophylaxis (cardiovascular; vascular graft; breast; dialysis access; orthopedic; head, neck and thoracic; gastrointestinal; colorectal; appendectomy; hysterectomy; termination of pregnancy; renal transplantation; liver transplantation; muscular, skeletal and soft tissue trauma; endoscopic procedures; caesarean section); severe ulcers in diabetics; suppurative wound infections (surgical or traumatic, Gram negative bacilli suspected or proven)

Side Effects: pain and local reaction at injection site, hypersensitivity syndrome, fixed drug reaction, lupus erythematosus, photosensitivity, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; modify dosage in renal dysfunction (coagulopathy) and in dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

LORACARBEF: first generation oral cephalosporin; *Streptococcus pyogenes* highly susceptible, *Escherichia coli*, *Proteus mirabilis* and *Staphylococcus aureus* susceptible, *Klebsiella* moderately susceptible, *Pseudomonas aeruginosa* resistant

Side Effects: serum sickness-like illness

CEFACLOR: first generation moderate spectrum and *Haemophilus* active oral cephalosporin; not affected by food; similar activity to cephalothin and cephalexin but active against *Haemophilus influenzae* (< 5% resistance in Australia); spectrum also includes β-lactamase negative *Neisseria gonorrhoeae* (100% susceptible), *Neisseria meningitidis* (100% susceptible at 0.12 mg/L), *Shigella* (100% susceptible), *Staphylococcus aureus*, *Streptococcus agalactiae* (0.5 mg/L), *Streptococcus equinus* (100% susceptible at 0.25 mg/L), *Streptococcus pneumoniae*, *Streptococcus pyogenes* (100% susceptible at 0.5 mg/L); significant inoculum effect; half life 0.6 h; C_{max} 16.5 mg/L; bioavailability > 90%; renal excretion 75%; very expensive

Indications: has found role in treatment of acute cystitis in children, respiratory tract infection (bronchitis, acute bacterial otitis media, mild to moderate community acquired pneumonia due to resistant organism or slow response in adult > 60 y or with coexisting illness or in child 3 mo - 10 y with penicillin hypersensitivity, acute sinusitis), water-related infections in children and remote areas

Side Effects: hypersensitivity syndrome, serum sickness-like reaction; moderate risk of serious adverse reactions and gastrointestinal adverse effects, low risk of skin rash (pustulosis, Stevens-Johnson syndrome); requires dose adjustment in renal failure and dialysis; probably safe in pregnancy

CEPHAMANDOLE: parenteral second generation moderate spectrum and *Haemophilus* active cephalosporin; more stable to some Gram negative β-lactamases and more active against *Haemophilus influenzae* than first generation; similar activity against Gram positives to first generation; spectrum includes *Aeromonas hydrophila*, *Moraxella* (≤ 0.06-1 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Yersinia enterocolitica* (100% susceptible); resistance (and cross-resistance to other ß-lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; no to moderate postantibiotic effect; may show inoculum effect; CSF penetration 2-9%; mode of elimination renal; more expensive than first generation

Indications: limited role in therapy; bacteremia and septicemia due to *Anaerobiospirillum succiniciproducens*; severe *Haemophilus influenzae* pneumonia

Side Effects: hypoprothrombinemia, hemorrhage, hypersensitivity syndrome, pemphigus, serum sickness-like illness, Stevens-Johnson syndrome; coagulopathy in renal insufficiency (administer vitamin K supplement), rarely seizures and interstitial nephritis (modify dose interval); requires dose adjustment in dialysis; cephamandole-induced hypoprothrombinemia may enhance anticoagulant effect of warfarin and other oral anticoagulants; probably safe in pregnancy

CEFOXITIN: cephamycin but usually included in second generation cephalosporins; moderate spectrum and anaerobes; parenteral; less active than first generation against Gram positives, particularly *Staphylococcus aureus*; greater activity than cephamandole against *Bacteroides fragilis* (60-70% susceptible; cefoxitin and cefotetan only cephalosporins active against this species); spectrum includes *Actinomyces* (95-100% susceptible), *Aeromonas hydrophila*, anaerobic cocci (100% susceptible), *Arachnia* (95-100% susceptible), *Campylobacter gracilis* (100% susceptible), *Bacteroides uniformis* (100% susceptible), *Capnocytophaga canimorsus* (95% susceptible), *Eikenella corrodens* (95% susceptible), *Fusobacterium* (99% susceptible), *Moraxella catarrhalis* (< 0.06-0.25 mg/L), *Neisseria meningitidis* (0.12 mg/L), *Pasteurella multocida* (95% susceptible), methicillin susceptible *Staphylococcus aureus* (100% susceptible), *Streptococcus agalactiae* (100% susceptible), *Streptococcus canis* (1 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Streptococcus viridans* (100% susceptible); 25% bronchial penetration 2-3 h after 2 g i.v. dose; intraperitoneal penetration 85%; CSF penetration 1-35%; increased V_d in elderly; protein binding 70% (reduced in elderly); implicated in emergence of multiple drug resistance during therapy; no significant inoculum effect; mode of elimination renal; more expensive than first generation

Indications: limited role in therapy; has been used as prophylactic antibiotic for colorectal, appendicectomy, hysterectomy, termination of pregnancy, liver transplantation surgery and for treatment of septic arthritis due to *Neisseria*, cervical fascial space infections in normal patients, clostridial abortional and puerperal infection, disseminated gonococcal and meningococcal disease, pelvic inflammatory disease and associated acute peritonitis, peritonitis suspected associated with IUD, salpingitis and other gynecologic and obstetric infections, mycobacterial local and generalised sepsis; metronidazole provides superior cover against most anaerobes

Side Effects: hypersensitivity syndrome, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; coagulopathy (administer vitamin K supplement) and nephrotoxicity (interstitial nephritis; adjust dose interval appropriately, monitor renal function; may falsely elevate serum creatinine measurement by certain assays) and, rarely, seizures in renal insufficiency; dose adjustment required in dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

CEFOTETAN: parenteral second generation cephalosporin; moderate spectrum and anaerobes; less active than first generation against Gram positives, especially *Staphylococcus aureus*; similar activity to cefoxitin but longer half life; spectrum includes *Actinomyces* (95% susceptible), *Clostridium* (95% susceptible), *Enterobacter agglomerans* (MIC 0.12 mg/L), *Haemophilus influenzae* (0.5 mg/L), *Neisseria gonorrhoeae* (0.25 mg/L), *Neisseria meningitidis* (0.06 mg/L), *Peptostreptococcus* (100% susceptible), *Proteus mirabilis* (0.5-1 mg/L), *Providencia rettgeri* (0.25 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Streptococcus pyogenes* (1mg/L); covers 68% of *Bacteroides fragilis* group (cefotetan and cefoxitin only cephalosporins active against this group); intraperitoneal penetration 56%; protein binding 89%; implicated in emergence of multiple resistance during therapy; may show inoculum effect; more expensive than first generation

Indications: limited role in therapy; epiglottitis in immunocompromised; prophylaxis and treatment of mixed aerobic and anaerobic infections, especially those arising from gastrointestinal and genital tracts; septicemia; surgical prophylaxis (colorectal, appendicectomy, hysterectomy, termination of pregnancy, liver transplantation)
Side Effects: hypoprothombinemia, hemorrhage, hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome; disulfiram-like reaction with alcohol possible; dose interval adjustment required in renal failure and in dialysis; probably safe in pregnancy; cefotetan-induced hypoprothrombinemia may enhance anticoagulant effect of warfarin and other oral anticoagulants
CEFUROXIME: parenteral second generation cephalosporin; spectrum includes *Haemophilus influenzae* (MIC 0.2 mg/L), *Helicobacter pylori* (4 mg/L), *Moraxella catarrhalis* (2 mg/L), *Neisseria gonorrhoeae* (0.06 mg/L), *Proteus mirabilis* (1 mg/L), *Peptococcus* (2 mg/L), *Shigella* (4 mg/L), methicillin susceptible *Staphylococcus* (2 mg/L), *Streptococcus agalactiae* ($\leq$ 0.5 mg/L), *Streptococcus canis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (0.06-4 mg/L), *Streptococcus pyogenes* (0.03 mg/L); *Bacteroides, Clostridium difficile, Proteus vulgaris, Pseudomonas aeruginosa* resistant; no significant change in V_d but clearance reduced in elderly; implicated in emergence of multiple drug resistance; may show inoculum effect; CSF penetration 12-14%
Indications: bronchitis; epiglottitis and bacterial tracheitis in immunocompromised; large bowel and cardiothoracic surgical prophylaxis; beta-lactamase producing *Haemophilus influenzae* infections; *Staphylococcus aureus* or *Haemophilus influenzae* in 3 mo - 6 y.o.; cellulitis without evidence of trauma; sinusitis; septic arthritis
Side Effects: hypersensitivity syndrome, pemphigus, photosensitivity, pustulosis, serum sickness-like illness, Stevens-Johnson syndrome; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea
CEFUROXIME AXETIL: oral dosing schedule twice a day (with or after food); spectrum includes *Haemophilus influenzae*, *Moraxella catarrhalis*, *Proteus mirabilis* (++), *Staphylococcus aureus* (++), *Streptococcus pneumoniae*, *Streptococcus pyogenes* (+++); very expensive
Indications: gonorrhoea; acute otitis media
Side Effects: low risk of serious adverse reactions, skin rash; moderate risk of gastrointestinal adverse effects
CEFORANIDE: parenteral second generation cephalosporin; implicated in emergence of multiple drug resistance
CEFONICID: parenteral second generation cephalosporin; strongly affected by type I β-lactamase; moderate inducer of type I β-lactamase; implicated in emergence of multiple drug resistance
Side Effects: hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome
CEFOTIAM: spectrum includes *Streptococcus pneumoniae* (MIC < 0.12 mg/L), *Streptococcus pyogenes* (< 0.12 mg/L)
Side Effects: autoimmune neutropenia in infants
CEFOTAXIME: broad spectrum third generation cephalosporin; parenteral; 25% bronchial penetration 2-3 h after 1 g i.m. dose; intraperitoneal penetration 92%; CSF penetration 0-54%; protein binding 55%; reduced clearance in elderly; extended spectrum of activity covering majority of community-acquired enteric Gram negative bacilli; less active against Gram positive organisms than first and second generation; not active against *Enterococcus* or methicillin resistant *Staphylococcus aureus*; greater penetration into CSF than earlier cephalosporins; covers only 20-50% of *Pseudomonas* strains and 33% of *Bacteroides fragilis* group; spectrum includes *Aeromonas hydrophila*, anaerobic cocci (100% susceptible), *Clostridium* (85% susceptible), *Escherichia coli* (0.1% resistant in Australia), *Fusobacterium* (90% susceptible), *Haemophilus influenzae* (0.6% resistance in Australia), *Klebsiella oxytoca* (96% of hospital isolates), *Klebsiella pneumoniae* (6% resistance in Australia), *Legionella* ($\leq$ 0.12-0.5 mg/L), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), other *Moraxella* (< 0.06-0.25 mg/L), penicillinase positive *Neisseria gonorrhoeae* (0.01-0.03 mg/L), *Neisseria meningitidis* (0.06 mg/L), *Proteus mirabilis* (0.5% resistant in Australia), *Salmonella* (< 0.003-0.6 mg/L), *Shigella* (0.03-0.06 mg/L), *Staphylococcus aureus* (98% susceptible), *Streptococcus agalactiae* (0.01-0.25 mg/L), *Streptococcus canis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (resistance not yet confirmed in Australia), *Streptococcus pyogenes* (< 1 mg/L), *Streptococcus viridans* (0.5 mg/L), *Yersinia* (0.06-0.25 mg/L); in Australia, *Enterobacter* 52% resistant due to β-lactamase; resistance (and cross-resistance to other β-lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; strongly affected by type I β-lactamase; slight inducer of type I β-lactamase; inactivated by plasma-mediated extended spectrum β-lactamases; may show inoculum effect; mode of elimination hepatic
Indications: many more times expensive than gentamicin and use should be restricted to broad Gram negative coverage in renally impaired patients and in intensive care areas (69-94% cure rate in Gram negative pneumonia, 87% cure rate in osteomyelitis, 90% cure rate in other serious infections); severe bite and clenched fist injuries; treatment of hospital acquired meningitis and meningitis due to enteric Gram negative bacilli, *Haemophilus influenzae*, *Neisseria* or *Streptococcus* in penicillin hypersensitive or relatively resistant *Streptococcus pneumoniae;* pediatric invasive *Haemophilus influenzae* type b infections; single dose therapy for gonorrhoea; septic arthritis due to unknown organism in < 5 year old; cholangitis and cholecystitis; fish spine injury and other water-related infections due to *Aeromonas* or *Vibrio;* hepatic abscess; pancreatitis due to coliforms; pancreatic abscess; peritonitis of suspected bowel origin; pneumonia (severe community acquired, mild to moderate community acquired due to resistant organisms or slow response in child 3 w - 3 mo, mild to moderate nosocomial

with no specific risk factors in penicillin hypersensitive with significant renal failure); complicated or severe acute sinusitis; Lyme disease, especially with rheumatologic, neurologic or cardiac involvement; also used for bacteremia and septicemia (infection from genital tract in elderly or diminished renal function, infection from respiratory system, focus from biliary or gastrointestinal tract in elderly patients with diminished renal function or significantly elevated serum creatinine, focus probably urinary tract in penicillin hypersensitive, children < 5 y with facial or periorbital cellulitis, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer in elderly or diminished renal function, unidentified source in child, due to *Neisseria meningitidis*); brain and epidural abscess; severe cellulitis due to *Haemophilus influenzae*; cerebrospinal fluid shunt infection due to aerobic Gram negative bacilli; cervical fascial space infections in immunocompromised; purulent conjunctivitis due to penicillinase-producing *Neisseria gonorrhoeae*; acute cystitis due to *Klebsiellla*; deep fascial space infections in immunocompromised; disseminated gonococcal and meningococcal disease; endocarditis due to *Haemophilus influenzae*, *Eikenella corrodens*, *Corynebacterium*; epiglottitis in normal host; penetrating eye injuries when clindamycin not available; sexually acquired pelvic sepsis and pelvic inflammatory disease in inpatient; perinatal generalised disease due to penicillinase-producing *Neisseria gonorrhoeae*; spontaneous peritonitis; peritonsillar abscess in immunocompromised; pneumonia (coliform, severe and moderate community acquired in patients with chronic lung disease, diabetics, alcoholics, nosocomial, aspiration, severe *Haemophilus influenzae*, *Acinetobacter*); preseptal and postseptal cellulitis; pulmonary abscess; severe acute pyelonephritis if aminoglycoside undesirable

Side Effects: local reactions in 5%, hypersensitivity, serum sickness-like illness, Stevens-Johnson syndrome, hematological effects, gastrointestinal effects (including pseudomembranous colitis), increases in serum transaminases, alkaline phosphatase, creatinine, blood urea; moderate to significant adjustment of dosage interval in renal failure (rarely, seizures and interstitial nephritis) and in dialysis; probably safe in pregnancy

Moxalactam (Latamoxef): third generation cephalosporin; parenteral; covers only about 20-50% of *Pseudomonas* strains but 73% of *Bacteroides fragilis* group; resistance (and cross-resistance to other β-lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; moderately affected by type I β-lactamase; low inducer of type I β-lactamase; intraperitoneal penetration 70%; CSF penetration 12%; protein binding 50%; increased V_d, reduced clearance in elderly; may show inoculum effect; withdrawn due to low usage because of uncommon, but important, tendency to cause bleeding in patients with poor nutritional state

Cefoperazone: third generation cephalosporin; parenteral; covers 70-90% of *Pseudomonas* strains but only 4% of *Bacteroides fragilis* group; spectrum includes *Aeromonas hydrophila*, anaerobic cocci (100% susceptible), *Haemophilus influenzae* (< 1 mg/L), *Hafnia alvei* (100% susceptible), *Neisseria gonorrhoeae* (< 1 mg/L), *Neisseria meningitidis* (0.008-0.12 mg/L), *Peptostreptococcus* (≤ 1 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Serratia marcescens* (0.06 mg/L), *Streptococcus agalactiae* (0.25 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Yersinia enterocolitica* (100% susceptible); considerably longer half life than other members of group except ceftriaxone; strongly affected by type I β-lactamase; no to moderate postantibiotic effect; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect; CSF penetration 3-6%

Indications: use should be restricted to treatment of Gram negative meningitis due to Enterobacteriaceae or of organisms resistant to first and second generation cephalosporins in which aminoglycoside therapy is not indicated; cure rate in Gram negative pneumonia 68-94%

Side Effects: coagulopathy (hypoprothrombinemia in 4-66% and hemorrhage in 0.5-8%), especially in renal insufficiency (administer vitamin K supplement), hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome

Ceftizoxime: third generation cephalosporin; parenteral; covers only 34% of *Bacteroides fragilis* group; spectrum includes anaerobic cocci (100% susceptible), *Escherichia coli* (MIC < 1 mg/L), *Fusobacterium* (94% susceptible), *Klebsiellla* (< 1 mg/L), *Proteus mirabilis* (< 1 mg/L), *Shigella* (< 1 mg/L), *Streptococcus canis* (100% susceptible at ≤ 0.015 mg/L), *Streptococcus pneumoniae* (< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L); implicated in emergence of multiple drug resistance during therapy; shows inoculum effect; CSF penetration 23%

Indications: appendicitis; cervical fascial space infections in immunocompromised; cranial parameningeal deep fascial space infections in immunocompromised; Gram negative pneumonia (66-100% cure rate); other serious Gram negative infections (89% cure rate)

Side Effects: erythema nodosum, serum sickness-like illness, Stevens-Johnson syndrome

Ceftriaxone: broad spectrum third generation cephalosporin; parenteral (i.m. or i.v. daily dose); considerably higher half life than other members of group except cefoperazone; almost identical spectrum to cefotaxime but different pharmacology; spectrum includes *Borrelia burgdorferi* (MIC 0.01-1 mg/L), *Clostridium perfringens* (≤ 1 mg/L), *Escherichia coli* (0.1% resistant in Australia), *Haemophilus influenzae* (0.6% resistant in Australia), *Klebsiella oxytoca* (94% of hospital isolates), *Klebsiella pneumoniae* (6% resistant in Australia), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), *Neisseria gonorrhoeae* (resistance not yet reported), *Neisseria meningitidis* (resistance not yet reported), *Peptostreptococcus* (≤ 1 mg/L), *Proteus mirabilis* (100%), *Pseudomonas acidovorans* (0.5 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Salmonella* (0.01-0.19 mg/L), *Shigella* (< 1 mg/L), *Streptococcus canis* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae*

(< 1 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Yersinia* (0.06-0.12 mg/L); in Australia, *Enterobacter cloacae* 40% resistant; resistance (and cross-resistance to other β-lactam antibiotics and aminoglycosides) may develop during treatment of *Pseudomonas aeruginosa*, *Serratia*, *Citrobacter* and *Enterobacter*; covers only 26% of *Bacteroides fragilis* group; strongly affected by type I β-lactamase; low inducer of type I β-lactamase; inactivated by plasma-mediated extended spectrum β-lactamases; no significant change in V_d, reduced protein binding in elderly; CSF penetration 2-7%; in WHO Model List of Essential Drugs

Indications: many times more expensive than gentamicin and use should be restricted; septic arthritis (due to *Neisseria*, *Haemophilus influenzae*, *Eikenella corrodens*; organism unknown, < 5 y); bacteremia and septicemia (infection from female genital tract in elderly or diminished renal function, infection from respiratory system, focus probably biliary or gastrointestinal tract in elderly patients with diminished renal function or significantly elevated serum creatinine, focus probably urinary tract in penicillin hypersensitive, children < 5 y with facial or periorbital cellulitis, focus probably decubitus or ischemic ulcer or diabetic foot ulcer in elderly or diminished renal function, focus probably intravascular catheter in elderly or diminished renal function, unidentified source in child or remote areas, due to *Neisseria meningitidis*); severe cat and dog and human bite and clenched fist injury infections; chancroid; cholangitis and cholecystitis; purulent conjunctivitis due to penicillinase-producing *Neisseria gonorrhoeae*; disseminated gonococcal and meningococcal disease; bacterial dysentery; endocarditis due to *Escherichia coli*; enteric fever; sexually acquired acute epididymitis and epididymoorchitis; epiglottitis; penetrating eye injuries when clindamycin not available; fish spine injury and other water-related infections due to *Aeromonas* or *Vibrio;* gonorrhoea; hepatic abscess; Lyme disease (arthritis, meningoencephalitis, heart block); meningitis (hospital acquired and due to enteric Gram negative bacilli or to *Neisseria* or *Streptococcus* in penicillin hypersensitive, relatively resistant *Streptococcus pneumoniae*, *Haemophilus influenzae*); meningococcal and *Haemophilus influenzae* type b meningitis prophylaxis in pregnant; osteomyelitis and osteochondritis; pancreatitis due to coliforms; pancreatic abscess; sexually acquired pelvic sepsis and pelvic inflammatory disease in inpatient; peritonitis (spontaneous, suspected bowel origin); peritonsillar abscess in immunocompromised; pneumonia (*Haemophilus influenzae*, coliform (66-94% cure rate), mild to moderate community acquired with risk factors or due to resistant organisms or slow response in child 3 w - 3 mo, moderate community acquired in patient with risk factors in remote areas, severe community acquired, mild to moderate nosocomial with no specific risk factors in penicillin hypersensitive with significant renal failure); other serious Gram negative infections (87% cure rate); preseptal and postseptal cellulitis; pulmonary abscess; severe acute pyelonephritis if aminoglycoside undesirable; rape prophylaxis; complicated or severe acute sinusitis; surgical prophylaxis; syphilis prophylaxis; gonococcal vaginitis (β-lactamase positive)

Side Effects: hypersensitivity syndrome, pemphigus, serum sickness-like illness, Stevens-Johnson syndrome; coagulopathy in renal insufficiency (administer vitamin K supplement); reversible pseudolithiasis or biliary sludge formation; hyperprothrombinemia and enhanced anticoagulant effect of warfarin and other oral anticoagulants; dose adjustment not required in dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

CEFSULODIN: third generation cephalosporin; binds chiefly to PBP1a; specific activity against *Pseudomonas aeruginosa* and Gram positive cocci other then *Enterococcus* but little activity against Enterobacteriaceae; implicated in emergence of multiple resistance during therapy

CEFMENOXIME: third generation cephalosporin; covers only 18% of *Bacteroides fragilis* group; spectrum includes *Citrobacter diversus* (MIC 0.12 mg/L), *Enterobacter aerogenes* (0.25-1 mg/L), *Escherichia coli* (0.06-0.13 mg/L), *Klebsiella oxytoca* (0.12-1 mg/L), *Klebsiella pneumoniae* (< 0.12 mg/L), *Proteus mirabilis* (≤ 0.01 mg/L), *Providencia stuartii* (0.06-1 mg/L), *Salmonella* (≤ 0.12 mg/L), *Streptococcus pneumoniae* (0.01-0.06 mg/L), *Streptococcus pyogenes* (0.01-0.03 mg/L), *Yersinia* (0.06-0.25 mg/L); no significant effect on V_d, reduced clearance in elderly; implicated in emergence of multiple drug resistance during therapy; no inoculum effect; CSF penetration 6-19%

CEFAZAFLUR: minimal inoculum effect

CEFBUPERAZONE: spectrum includes *Citrobacter diversus* (MIC 0.12-0.25 mg/L), *Klebsiella oxytoca* (0.25-1 mg/L), *Klebsiella pneumoniae* (0.25-0.5 mg/L)

CEFIXIME: oral third generation cephalosporin; oral dosing schedule 4 times a day; expensive; spectrum similar to parenteral third generation cephalosporins; includes *Citrobacter diversus* (100% susceptible at ≤ 0.5 mg/L), *Escherichia coli* (MIC 0.25-32 mg/L), *Haemophilus influenzae* (0.06-0.12 mg/L), *Klebsiella oxytoca* (0.54 mg/L), *Klebsiella pneumoniae* (0.25 – > 64 mg/L), *Moraxella catarrhalis* (0.25-0.5 mg/L), *Neisseria gonorrhoeae* (0.015 mg/L), *Neisseria meningitidis* (100% susceptible at ≤ 0.06 mg/L), *Proteus mirabilis* (100% susceptible at ≤ 0.2 mg/L), *Proteus vulgaris* (0.015-0.25 mg/L), *Providencia rettgeri* (100% susceptible at 0.5 mg/L), *Providencia stuartii* (100% susceptible at ≤ 0.25 mg/L), *Deltfia acidovorans* (0.5 mg/L), *Salmonella* (1 mg/L), *Streptococcus agalactiae* (0.5 mg/L), penicillin-susceptible *Streptococcus pneumonia* (0.5 mg/L), *Streptococcus pyogenes* (0.5 mg/L); anaerobes, *Enterococcus*, *Helicobacter pylori, Pseudomonas aeruginosa*, *Serratia marcescens, Shigella, Staphylococcus* 100% resistant

Side Effects: low risk of serious adverse reactions (hypersensitivity syndrome, serum sickness-like illness), skin rash (Stevens-Johnson syndrome); moderate risk of gastrointestinal adverse effects

CEFPIRAMIDE: spectrum includes *Klebsiella oxytoca* (MIC 0.1-0.5 mg/L), *Streptococcus pneumoniae* (0.02-0.25 mg/L), *Streptococcus pyogenes* (0.02-0.25 mg/L)

CEFODIZIME: spectrum includes *Escherichia coli* (MIC 1 mg/L), *Klebsiella oxytoca* (0.5 mg/L), *Serratia marcescens* (0.1-0.2 mg/L)

Side Effects: high risk of substantial renal function derangement on simultaneous infusion with vancomycin, especially in diabetics

CEFETAMET PIVOXIL: oral third generation cephalosporin (take with or after food); *Streptococcus pyogenes* and *Proteus mirabilis* highly susceptible, *Escherichia coli* and *Klebsiellla* susceptible, *Staphylococcus aureus* and *Pseudomonas aeruginosa* resistant

CEFPODOXIME PROXETIL: oral broad spectrum (similar to parenteral third generation) third generation cephalosporin (take with or after food (absorption increased)); increased pH (antacids, H_2-antagonists) reduces bioavailability; *Streptococcus pyogenes* and *Proteus mirabilis* highly susceptible, *Escherichia coli* and β-lactamase-producing *Haemophilus influenzae* susceptible, *Klebsiella* moderately susceptible, *Staphylococcus aureus* and *Pseudomonas aeruginosa* resistant

Indications: upper and lower respiratory tract infections due to streptococci, *Haemophilus influenzae*, *Moraxella catarrhalis;* skin and soft tissue infections; urinary tract infections

Side Effects: diarrhoea, nausea, chest pain, hypotension, rash, pseudomembranous colitis, anaphylactic shock, hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome; probably safe in pregnancy; requires dosage interval adjustment in renal failure and in dialysis

CEFTIBUTEN: oral (once daily) highly β-lactamase stable third generation cephalosporin; spectrum includes *Escherichia coli* (MIC 0.25-12 mg/L), *Haemophilus influenzae* (0.03-0.5mg/L), *Helicobacter pylori* (8 mg/L), *Klebsiella oxytoca* (0.06 mg/L), *Klebsiella pneumoniae* (0.12 - >64 mg/L, *Moraxella catarrhalis* (2-4 mg/L), *Proteus vulgaris* (0.03 mg/L), *Neisseria gonorrhoeae* (0.015-0.13 mg/L), *Salmonella* (0.06 mg/L), *Serratia marcescens* (4-8 mg/L), *Shigella* (0.25 mg/L), *Streptococcus pyogenes* (0.5 mg/L); *Pseudomonas aeruginosa,* anaerobes and Gram positives other than *Streptococcus pyogenes* and some strains of penicillin-susceptible *Streptococcus pneumoniae* resistant

Side Effects: diarrhoea (infrequent, usually mild), hypersensitivity syndrome, serum sickness-like illness, Stevens-Johnson syndrome

CEFPIROME: broad spectrum and antipseudomonal third generation parenteral cephalosporin; spectrum includes *Escherichia coli* (MIC 0.03-0.12 mg/L), *Haemophilus influenzae* (0.06 mg/L), *Klebsiella* (0.03-0.25 mg/L), *Neisseria gonorrhoeae* (0.01-0.03 mg/L), *Proteus mirabilis* (0.01-0.12 mg/L), *Pseudomonas aeruginosa, Salmonella* (0.06-0.12 mg/L), *Shigella* (0.01-0.03 mg/L), methicillin susceptible *Staphylococcus aureus* (0.5-1 mg/L), *Streptococcus agalactiae* (0.01-0.06 mg/L), *Streptococcus pneumoniae* (0.01-0.25 mg/L), *Streptococcus pyogenes* (0.02-0.25 mg/L), *Yersinia* (≤ 0.25 mg/L)

Side Effects: local phlebitis, thrombophlebitis and pain, hypersensitivity, gastrointestinal (including pseudomembranous colitis), increased liver enzyme serum levels, rare cholestatic jaundice, increased serum creatinine, hematological effects, headache, dizziness, hemorrhage, ecchymosis, altered rhythm, dyspnea, malaise, superinfection; safety in pregnancy not established; requires dose adjustment in renal failure and in dialysis

CEFTAZIDIME: broad spectrum and antipseudomonal parenteral third generation cephalosporin; stability to most β-lactamases (but susceptible to extended spectrum β-lactamases and resistance due to chromosomal β-lactamases may develop during therapy) and ease of use attractive features; less active against Gram positive organisms than cefepime and cefpirome; covers 96% of Enterobacteriaceae, 86% of nonenteric Gram negative bacilli (including 70-90% of *Pseudomonas* strains), 67% of staphylococci and 93% of nonenterococcal streptococci but < 1% of *Enterococcus*; spectrum includes *Burkholderia cepacia, Escherichia coli* (99% of hospital isolates), *Haemophilus influenzae* (MIC 0.06-0.125 mg/L), *Klebsiella oxytoca* (98% of hospital isolates), *Klebsiella pneumoniae* (94% of hospital isolates), *Moraxella catarrhalis* (resistance not yet confirmed in Australia), *Neisseria gonorrhoeae* (0.01-0.06 mg/L), *Proteus mirabilis* (100%), *Pseudomonas aeruginosa* (10% resistance in Australia), *Salmonella* (0.06-0.5 mg/L), *Streptococcus agalactiae* (0.25-0.5 mg/L), *Streptococcus canis* (0.125 mg/L), *Streptococcus pneumoniae* (0.12-0.5 mg/L), *Streptococcus pyogenes* (< 1 mg/L), *Yersinia* (0.12-0.5 mg/L); only cephalosporin active against *Stenotrophomonas maltophilia* (92% of hospital isolates); in Australia, *Enterobacter cloacae* 61% resistant; serum protein binding 17%; reduced clearance in elderly; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect; CSF penetration 14%; in WHO Model List of Essential Drugs

Indications: many times more expensive than gentamicin and use should be restricted to infections (including bacteremia and septicemia) in febrile neutropenic patients (Gram negative pneumonia cure rate 66-94%, other serious Gram negative infections 84% cure rate); melioidosis (including bacteremia and septicemia); severe community acquired pneumonia in adult with bronchiectasis or cystic fibrosis; severe nosocomial pneumonia; *Klebsiella pneumoniae* pneumonia; *Pseudomonas* infection (including bacteremia and septicemia) in penicillin hypersensitive patient or patient at increased risk for aminoglycoside toxicity; endophthalmitis; perianal and perirectal abscess and cellulitis in patients with malignant disease; *Pseudomonas aeruginosa* meningitis

Side Effects: occasional urticarial rash, bullous pemphigoid, pemphigus, photosensitivity, Stevens-Johnson syndrome, local reaction, hypersensitivity, serum sickness-like illness, gastrointestinal (including pseudomembranous colitis), headache,

dizziness, neurological sequelae in patients with renal impairment, candidiasis, rise in liver enzymes; dose adjustment required in renal failure and dialysis; probably safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea

CEFEPIME: broad spectrum and antipseudomonal parenteral 'fourth generation' cephalosporin; similar activity to cefotaxime but improved coverage of *Pseudomonas aeruginosa, Enterobacter, Serratia* and methicillin resistant *Staphylococcus aureus;* spectrum includes *Escherichia coli* (MIC 0.03-0.12 mg/L), *Haemophilus influenzae* (0.01-0.12 mg/L), *Klebsiella* (0.01-0.12 mg/L), *Neisseria gonorrhoeae* (0.01-0.03 mg/L), *Proteus mirabilis* (0.03-0.06 mg/L), *Salmonella* (0.03-0.2 mg/L), *Shigella* (0.01-0.06 mg/L), *Streptococcus agalactiae* (0.01-0.06 mg/L), *Streptococcus pneumoniae* (0.01-0.06 mg/L); more active against Gram positives than ceftazidime; susceptible to extended spectrum β-lactamases and chromosomal cephalosporinases

Indications: treatment of severe community- or hospital-acquired infections that are documented or suspected to involve resistant aerobic Gram negative bacteria, including Enterobacteriaceae, *Haemophilus influenzae* and *Pseudomonas*; empiric therapy for febrile neutropenia

Side Effects: hypersensitivity syndrome, Stevens-Johnson syndrome; probably safe in pregnancy; dose adjustment required in renal impairment

CEFDITOREN: oral third generation aminothiazolyl cephalosporin active against *Haemophilus influenzae, Moraxella catarrhalis, Streptococcus penumoniae,* methicillin susceptible *Staphylococcus aureus;* not active against *Bacteroides fragilis, Chlamydophila pneumoniae, Legionella, Mycoplasma pneumoniae, Pseudomonas aeruginosa*

Indications: acute exacerbation of chronic bronchitis, pharyngitis/tonsillitis, uncomplicated skin and skin structure infections

Side Effects: diarrhoea, nausea, vomiting, headache, dyspepsia

Contraindications: hypersensitivity to penicillins, cephalosporins, milk protein; carnitine deficiency

CEFTOBIPROLE: interferes with penicillin binding protein-mediated cell wall synthesis, leading to cell lysis; bactericidal; time/MIC best predictive parameter; primarily renal elimination

Side Effects: taste disturbance; cross-hypersensitivity with other β-lactams

MONOBACTAMS

AZTREONAM: monobactam; binds chiefly to PBP3; kills only growing organisms; inhibits class I cephases; relatively inactive against Gram positive organisms (only 1% of staphylococci, 0.1% of *Enterococcus* and 4% of other streptococci susceptible) and anaerobes but highly active against majority of aerobic Gram negative bacteria including β-lactamase-producing *Haemophilus influenzae* (MIC 0.016-0.25 mg/L), Enterobacteriaceae (97% susceptible) and nonenteric Gram negative bacilli (68% susceptible, including *Pseudomonas* resistant to aminoglycosides); spectrum includes *Escherichia coli* (99% of hospital isolates), *Haemophilus influenzae*, *Klebsiella oxytoca* (94% of hospital isolates), *Klebsiella pneumoniae* (93% of hospital isolates), *Morganella morganii* (100%), *Neisseria meningitidis*, *Proteus mirabilis* (100%), *Pseudomonas fluorescens*, *Salmonella* (≤ 0.12 mg/L); no significant change in V_d, protein binding or clearance in elderly; implicated in emergence of multiple drug resistance during therapy; shows inoculum effect

Indications: shows promise as an aminoglycoside substitute but high cost has restricted use to people with severe penicillin hypersensitivity or at increased risk for aminoglycoside toxicity; superior efficacy to aminoglycosides in treating bacteremia involving aerobic Gram negatives; Gram negative bacterial meningitis (86% cure rate); neonatal sepsis; *Klebsiella pneumoniae* pneumonia; *Haemophilus influenzae* pulmonary infection in cystic fibrosis

Side Effects: rash (common), phlebitis and thrombophlebitis at injection site (common), rare reduction in platelet count and anemia, rare jaundice and hepatitis, gastrointestinal effects (diarrhoea, nausea, vomiting common; gastrointestinal bleeding, abdominal cramps and bloating uncommon; pseudomembranous colitis rare), abnormal taste (common), elevated transaminases (transient common, significant rare), eosinophilia (common), headache (uncommon), dizziness (uncommon), mild local reactions, oral ulceration (uncommon), anaphylaxis (rare), angiedema (rare), bronchospasm (rare), shock (rare), neutropenia (rare), prolonged bleeding time (rare); probably safe in pregnancy; dose adjustment required in renal failure and dialysis; can be given to people with severe penicillin hypersensitivity as there is little cross sensitisation; theoretical possibility of enhanced warfarin effect

CARUMONAM: monobactam; 98% of Enterobacteriaceae and 75% of nonenteric Gram negative bacilli susceptible, but only 1% of staphylococci, 0.3% of *Enterococcus* and 8% of streptococci; spectrum includes *Citrobacter diversus* (MIC ≤ 0.12 mg/L), *Enterobacter aerogenes* (0.12-0.5 mg/L), *Escherichia coli* (0.06-0.12 mg/L), *Klebsiella oxytoca* (0.12-0.5 mg/L), *Klebsiella pneumoniae* (0.12-0.25 mg/L), *Morganella morganii* (≤ 0.12 mg/L), *Proteus mirabilis* (≤ 0.01 mg/L), *Salmonella* (≤ 0.12 mg/L), *Yersinia* (0.25-1 mg/L)

BACITRACIN: polypeptide mixture; inhibits dephosphorylation of lipid pyrophosphate thus impairing regeneration of lipid carrier; bactericidal; acts only on proliferating bacteria; active against Gram positive bacteria; diminishes phagocytosis

Indications: hordeolum (topical), skin infections (topical), *Clostidium difficile*-associated diarrhoea (oral)

Side Effects: allergic contact dematitis

GLYCOPEPTIDES: active against wide range of Gram positive organisms; Gram negatives not susceptible

Indications: treatment and prophylaxis of methicillin resistant staphylococcal infection, severe infections with susceptible organisms in penicillin hypersensitive

Side Effects: itch, fever, chills, eosinophilia, pain, erythema, thrombophlebitis, nephrotoxicity uncommon; anaphylaxis, superinfection, thrombocytopenia, leucopenia, neutropenia, tinnitus, dizziness, ototoxicity, toxic epidermal necrolysis rare

VANCOMYCIN (VANCOCIN): glycopeptide; binds to terminal residues of peptidoglycan, inhibiting peptidoglycan synthetase and polymerisation of linear peptide and thus cell wall synthesis; parenteral (i.v. infusion over at least an hour) and oral (treatment of pseudomembranous colitis only; relationship of dose to food doesn't matter); poor oral absorption; distributes into total body weight; limited CNS and pulmonary penetration; kills non-growing organisms; increased V_d, no significant change in protein binding, reduced clearance in elderly; moderate postantibiotic effect; slowly bactericidal; time-dependent killing; AUC:MIC may be best predictive parameter; active against Gram positive bacteria, including *Bacillus* (< 5% resistance in Australia), *Corynebacterium* (resistance not yet reported), *Micrococcus* (< 5% resistance in Australia), methicillin resistant staphylococci (*S.aureus* resistance reported from Japan and Slovak Republic; not yet confirmed in Australia; coagulase negative staphylococci < 5% resistance in Australia), *Streptococcus* (*S.mitis* resistance reported from USA and Europe); in Australia, *Enterococcus faecalis* 0.7% resistant, *Enterococcus faecium* 29% resistant; in USA, *Enterococcus* 14% resistant; kills bacteria phagocytosed by granulocytes; minimal inoculum effect; decreased bactericidal and bacteriostatic effect under anaerobic conditions; not active against Gram negative organisms; mode of elimination renal; in WHO Model List of Essential Drugs

Indications: increasing role in treatment of serious Gram positive infections (predominantly organisms resistant to β-lactams, methicillin resistant *Staphylococcus* or penicillin hypersensitive patients); reactive arthritis due to *Clostridium difficile*; septic arthritis due to methicillin resistant *Staphylococcus aureus*; bacteremia and septicemia (focus probably intravascular catheter; febrile neutropenic patients with *Staphylococcus* suspected, hospital acquired or vascular catheter infection or febrile after 3 d; due to methicillin resistant *Staphylococcus aureus*, *Bacillus, Rothia mucilaginosa, Corynebacterium jeikeium, Corynebacterium striatum, Corynebacterium urealyticum, Enterococcus*); severe streptococcal and staphylococcal cellulitis in penicillin hypersensitive; cerebrospinal fluid shunt infections due to *Staphylococcus*, *Enterococcus*, diphtheroids, *Propionibacterium*; cranial parameningeal deep fascial space infections following cranial surgery in immunocompromised; acute cystitis due to *Corynebacterium urealyticum;* endocarditis prophylaxis and treatment in penicillin hypersensitive; endophthalmitis; penetrating eye injuries; hospital acquired meningitis; postneonatal pyogenic meningitis due to penicillin resistant *Streptococcus pneumoniae*, *Staphylococcus*; mycotic aneurism; myocarditis and pericarditis due to *Staphylococcus aureus*; osteomyelitis and osteochondritis due to methicillin resistant *Staphylococcus aureus*; progressive perianal and perirectal abscess and cellulitis in patients with malignant disease; peritonitis (continuous ambulatory peritoneal dialysis, *Rothia mucilaginosa*); pneumonia (methicillin resistant *Staphylococcus aureus*, *Corynebacterium pseudodiphtheriticum,* severe community acquired in children < 10 y or with MRSA suspected or proven, mild to moderate nosocomial in patient with diabetes, coma or head injury and MRSA suspected or proven); prosthetic implants prophylaxis; pseudomembranous colitis and antibiotic-associated diarrhoea due to *Clostridium difficile* and unresponsive to metronidazole (oral); acute pyelonephritis with Gram positive cause in penicillin hypersensitive patient; septicemia; localised skin lesions due to methicillin resistant *Staphylococcus aureus*, *Corynebacterium jeikeium, Corynebacterium urealyticum, Corynebacterium striatum*; splenic abscess due to *Clostridium difficile*; surgical prophylaxis (cardiac surgery, arterial reconstructive surgery of abdominal aorta or lower limb, breast, dialysis access, craniotomy); systemic infections in granulocytopenia (breakthrough bacteremia, catheter-associated infection); toxic shock syndrome due to methicillin resistant *Staphylococcus aureus;* vascular graft infection

Side Effects: nephrotoxicity (particularly with concomitant aminoglycoside, aciclovir, amphotericin, cyclosporin, frusemide, cefodizime, cidofovir), otoxicity, 'red man' syndrome (rare infusion rate-dependent induction of histamine-mediated effects; prior administration of hydroxyzine gives protection, while diphenhydramine aborts it), bullous pemphigoid, hypersensitivity syndrome, lupus erythematosus, pustulosis, Stevens-Johnson syndrome, vasculitis, immune thrombocytopenia; delayed onset neutropenia in renal insufficiency; increased risk of neutropenia with zidovudine; thrombocytopenia; uncommon mild gastrointestinal tract disturbances with oral; cholestyramine may bind to oral and reduce antibacterial activity; modify dosage interval, monitor serum levels (even in hemodialysis patients), monitor renal function in renal dysfunction; safety in pregnancy not established; safe in breastfeeding; dose interval adjustment required in continuous venovenous and arteriovenous hemodialysis; toxic level > 10 mg/L trough, > 40 mg/L peak (monitor routinely at least once during a course of therapy); incompatible with benzylpenicillin, chloramphenicol, heparin, hydrocortisone, methicillin, novobiocin

TEICOPLANIN: glycopeptide related to vancomycin; similar spectrum to vancomycin but different pharmacology and, possibly, lower toxicity; i.m. and i.v. (slow injection or infusion)

Indications: as for vancomycin; endocarditis prophylaxis (bronchoscopy with rigid bronchoscope, dental procedures inducing gingival or mucosal bleeding, surgical procedures breaking respiratory mucosa, tonsillectomy and/or adenoidectomy in patients penicillin hypersensitive, on long-term penicillin or having taken β-lactam antibiotic more than once in previous month; cystoscopy, gall bladder surgery, esophageal dilatation, sclerotherapy for esophageal varices, surgical procedures breaking intestinal or genital mucosa, urethral catheterisation or urinary tract surgery in presence of urinary tract infection, urethral dilatation, vaginal delivery in presence of infection, vaginal hysterectomy in penicillin hypersensitive)

Side Effects: fever, rashes, nausea, vomiting, rigours, pruritis, diarrhoea, red man syndrome; modify dosage interval in renal failure and in continuous venovenous and arteriovenous hemodialysis (monitor levels to determine precise dosage requirements); safety in pregnancy and breastfeeding not established

Oritivancin: glycopeptide; binds to terminal residues of peptidoglycan, preventing crosslinking and inhibiting cell wall synthesis; bactericidal; concentration-dependent killing; poor oral absorption; highly protein bound; rapid tissue accumulation and prolonged retention; slow renal elminiation

Daptomycin: first lipopeptide agent; calcium-dependent insertion into bacterial cell membrane, leading to depolarization, DNA, RNA and protein synthesis arrest and eventual cell death; bactericidal; concentration-dependent killing; highly protein bound; distributes into total body weight; limited CNS penetration; inhibited by pulmonary surfactant; renal elimination

Side Effects: myopathy associated with elevated creatine phosphokinase elevation (reversible)

Dalbavancin: lipoglycopeptide; binds to terminal residues of peptidoglycan, preventinhg crosslinking and inhibiting cell wall synthesis; bactericidal; concentration-dependent killing; poor oral absorption; highly protein bound; renal and nonrenal elimination; long terminal half-life

Telavancin: lipoglycopeptide; binds to terminal resides of peptidoglycan, preventing crosslinking and inhibiting cell wall synthesis; interferes with bacterial cell wall membrane potential and permeability; bactericidal; concentration-dependent killing; poor oral absorption; highly protein bound; renal elimination

Side Effects: infusion reactions

Synercid: quinupristin + dalfopristin; i.v. streptogramin; active against Gram positive cocci including glycopeptide resistant enterococci (but poor activity against *Enterococcus faecalis*) and staphylococci

Indications: bloodstream infections with vancomycin resistant *Enterococcus faecium*, skin and skin structure infections due to methicillin susceptible *Staphylococcus aureus* or *Streptococcus pyogenes*

Side Effects: inflammation at infusion site in 42%, pain at infusion site in 40%, erythema and irritation at injection site common, arthralgia in 4-8%, nausea in 3-5%, myalgia in 1-5%; elevated transaminases, rash, vomiting, diarrhoea, headache, raised bilirubin common; fever, anaphylaxis, chest pain, pseudomembranous colitis, pancreatitis, peripheral edema, hypotension, gout, confusion, paresthesia, dizziness, hypertonia, insomnia, anxiety, leg cramps, dyspnea, pleural effusion, urticaria, tachycardia, jaundice, hepatitis, pharyngitis, oral candidiasis, stomatitis, anemia, thrombocytopenia, eosinophilia, raised blood urea and creatinine uncommon; interacts with P450 3A4 substrates (midazolam, nifedipine; increased risk of QT prolongation); increases risk of toxicity with cyclosporin, protease inhibitors, erythromycin; safety in pregnancy and breastfeeding not established

Pristinamycin: oral streptogramin active against Gram-positive bacteria, *Neisseria, Mycoplasma, Ureaplasma, Chlamydia, Haemophilus influenzae*

Coumermycin: bis-hydroxycoumarin; activity includes *Staphylococcus* (MIC $\leq$ 0.002-0.25 mg/L)

Colistin and Colistimethate: binds and disrupts membrane phospholipids by detergent action; bactericidal; active against bacteria irrespective of growth phase; weakly penetrates into mammalian cells and kills bacteria phagocytosed by granulocytes; active against Gram negative bacteria; spectrum includes *Bordetella bronchiseptica* (MIC 0.13-0.5 mg/L), *Enterobacter aerogenes, Escherichia coli, Haemophilus influenzae* (0.25-0.5 mg/L), *Klebsiella* (0.5 mg/L), *Pseudomonas aeruginosa*; colistin sulphate topical only; colistimethate sodium injectable prodrug of colistin

Indications: primarily used to treat *Pseudomonas* infection (especially topically in 'swimmer's ear'); now rarely used systemically

Side Effects: systemic: respiratory arrest, nephrotoxicity, paresthesia, hearing loss; modify dosage in renal dysfunction; maximum permissible blood level 5 mg/L; incompatible with cephalothin, erythromycin, hydrocortisone, lincomycin; potential for enhancement of neuromuscular blockade by aminoglycosides and curariform muscle relaxants; safety in pregnancy not established; caution in breastfeeding, monitor infant for diarrhoea

Polymyxin B: binds and disrupts phospholipids by detergent action; bactericidal; active against bacteria irrespective of growth phase; weakly penetrates into mammalian cells and kills bacteria phagocytosed by granulocytes; active against Gram negative bacteria

Indications: now rarely used systemically, except for multiresistant *Acinetobacter baumannii*; bacterial blepharitis (topical); more severe purulent conjunctivitis (topical); endotoxinemia; keratitis and iritis due to Gram negative bacilli (topical); otitis media prophylaxis (topical); folliculitis and paronychia due to *Pseudomonas aeruginosa*; ? useful in preventing septic shock in Gram negative bacteremia and septicemia

Side Effects: hypersensitivity reactions, gastrointestinal disturbances, skin reactions, dizziness, hearing loss, paresthesias, neuromuscular blockade, respiratory paralysis, nephrotoxicity, pain at injection site, visual disturbances, CNS toxicity in renal insufficiency (avoid use if possible or adjust dose appropriately); maximum permissible blood level 5 mg/L

Quinolones: bactericidal; anaerobes 100% intrinsic resistance

Nalidixic Acid: oral (relationship of dose to food doesn't matter) quinolone (quinoline carboxylic acid derivative); interferes with DNA template-RNA polymerase complex; active only against facultative Gram negative bacilli; spectrum includes *Aeromonas* (MIC 0.5 mg/L), *Campylobacter jejuni* (100% susceptible), *Haemophilus influenzae* (0.5 mg/L), *Neisseria*

meningitidis (0.5 mg/L), *Plesiomonas* (0.5 mg/L), but use virtually restricted to urinary tract infections; in WHO Model List of Essential Drugs as complementary drug for treatment of resistant shigellosis; mode of elimination renal
Indications: occasionally used in treatment of bacterial dysentery and urinary tract infection but several less toxic alternatives now available
Side Effects: gastrointestinal disturbances (nausea, vomiting, diarrhoea), skin reactions, photosensitivity, headache, precipitates convulsions in those predisposed, visual disturbances (glare reaction), bone marrow suppression, vestibular symptoms; avoid in renal dysfunction (CNS toxicity, seizures, ineffective in marked renal failure) and in dialysis; safe in pregnancy; may potentiate warfarin activity
4-QUINOLONES: includes fluoroquinolones; analogues of nalidixic acid with broader antibacterial activity, increased bactericidal effect, improved oral absorption and longer half lives; inhibit DNA synthesis by binding DNA gyrases; similar spectrum to aminoglycosides; only oral agents for treatment of *Pseudomonas*; also active against staphylococci (including methicillin resistant *Staphylococcus aureus*), borderline activity against *Streptococcus* and *Enterococcus*; close relation of MIC and MBC, with minor inoculum effect for most organisms; prolonged postantibiotic effect on staphylococci, Enterobacteriaceae and *Pseudomonas*; do not select resistant mutants of plasmid type; do not distort intestinal flora with respect to streptococci and anaerobic species; frequency of mutational resistance $\approx 10^{11}$; resistance has occurred where widely used in infections caused by *Staphylococcus aureus*, *Pseudomonas aeruginosa*, enteric Gram-negative bacilli, *Campylobacter* and *Neisseria gonorrhoeae*; generally do not select high level cross-resistant isolates to β-lactamases or aminoglycosides; kill bacteria phagocytosed by granulocytes; decreased bactericidal effect under anaerobic conditions; spectrum includes *Eikenella corrodens* (100% susceptible), *Neisseria gonorrhoeae* (2% low level and 2% high level resistance in Australia; 82% resistance in China, 69% high level resistance in the Philippines), *Pasteurella multocida* (95% susceptible), *Staphylococcus aureus*; anaerobes 100% intrinsic resistance; expensive
Indications: should be reserved for treatment of infections resistant to cheaper agents or where oral agent in essential
Side Effects: elevation of hepatic enzymes in 1.8-2.5%; nausea, vomiting, diarrhoea, abdominal pain, dyspepsia in 1-5%; skin effects (rash, itch) in 0.5-2%; eosinophilia in 0.2-2%; azotemia in 0.2-1.3%; dizziness, confusion, headache, insomnia in 0.1-0.3% (more likely in older patients); arthralgia, arthritis, myalgia, tendonitis, crystaluria, interstitial nephritis, insomnia, depression, QT interval prolongation uncommon; blood dyscrasias, hypoglycemia, psychotic reactions, convulsions, phototoxicity, colitis, anaphylaxis, elevated liver enzymes, hepatitis rare; arthropathies in young animals; possible CNS toxicity, nephropathy, ocular toxicity, tendon disorders (especially in elderly taking corticosteroids); rare risk of fever, rash, toxic epidermal hemolysis, Stevens-Johnson syndrome, vasculitis, serum sickness, allergic pneumonitis, acute renal insufficiency or failure, jaundice, acute hepatic necrosis or failure, anemia (including hemolytic and aplastic), thrombocytopenia (including thrombocytopenia purpure), leucopenia, agranulocytosis, pancytopenia, and other hematologic abnormalities after multiple doses; may antagonise polymyxin, chloramphenicol, erythromycin, rifampicin; aluminium, calcium, magnesium antacids, Asian dandelion, fennel seed, iron and zinc preparations, sucralfate, didanosine buffered preparations reduce plasma levels (space 2-6 h apart); phenytoin levels may be decreased, giving epileptogenic potential; increased anticoagulant effects with oral anticoagulants (rare but unpredictable); can markedly increase theophylline plasma levels
Contraindications: safety in pregnancy not established; use with caution in nursing mothers and children < 14 y
ACROSOXACIN: 4-quinolone
Indications: oral treatment of uncomplicated gonorrhoea
CINOXACIN: 4-quinolone; spectrum includes *Haemophilus influenzae* (MIC 1 mg/L)
ENOXACIN: 4-quinolone; oral (not affected by food); 40-78% penetration into blister fluid, 58-100% penetration into sputum and bronchial secretions, 35-50% penetration into bone, 18-21% penetration into prostatic tissue; spectrum includes aerobic Gram negative bacilli (MIC_{90} 1 mg/L), *Aeromonas* (100% susceptible), *Bacillus* (1 mg/L), *Bacteroides ureolyticus* (0.25 mg/L), *Bordetella pertussis* (0.25-0.5 mg/L), *Citrobacter amalonaticus* (97% susceptible at 0.25 mg/L), *Citrobacter diversus* (100% susceptible at 0.5 mg/L), *Citrobacter freundii* (98% susceptible at 0.5 mg/L), *Enterobacter aerogenes* (94% susceptible at 0.5 mg/L), *Enterobacter agglomerans* (94% susceptible at 0.5 mg/L), *Enterobacter cloacae* (0.8-1 mg/L), *Enterobacter sakazakii* (100% susceptible at 0.5 mg/L), Enterobacteriaceae (0.5-1 mg/L), *Escherichia coli* (0.5 mg/L), *Haemophilus influenzae* (≤ 0.004-0.5 mg/L), *Haemophilus paraprophilus* (0.06 mg/L), *Haemophilus parainfluenzae* (0.5 mg/L), *Hafnia alvei* (100% susceptible), *Legionella, Morganella morganii* (100% susceptible at 0.5 mg/L), various species of *Mycobacterium, Neisseria gonorrhoeae* (≤ 0.06-0.12 mg/L), *Neisseria meningitidis* (100% susceptible at < 0.12 mg/L), *Plesiomonas* (0.125-0.5 mg/L), *Proteus* (0.5-1 mg/L), *Delftia acidovorans* (1 mg/L), *Pseudomonas aeruginosa, Salmonella* (0.5 mg/L), *Serratia* (0.5 mg/L), *Shigella* (0.2-0.5 mg/L), *Staphylococcus haemolyticus* (1 mg/L), *Vibrio parahaemolyticus* (0.5 mg/L), *Yersinia enterocolitica* (0.25 mg/L); poor activity against streptococci, none against anaerobes
Indications: complicated urinary tract infection
Side Effects: nausea/vomiting in 6%, headache in 2%, dizziness in 2%, diarrhoea in 1%, abdominal pain in 1%, dyspepsia/flatulence in 1%, insomnia in 1%; mineral antacids, didanosine, H_2-antagonists, proton pump inhibitors, sucralfate reduce bioavailability; probenecid may reduce urinary excretion; may radically increase theophylline plasma levels; also

interacts with caffeine, some non-steroidal anti-inflammatory drugs (has resulted in seizures); safety in pregnancy not established

Contraindications: avoid if breastfeeding

Oxolinic Acid: 4-quinolone

Indications: used primarily in treatment of urinary infections

Ciprofloxacin: oral (take ½ to 1 h before food) and parenteral fluoroquinolone; achieves good serum, tissue and urine concentrations; serum protein binding 30%; no inoculum effect; 43-80% penetration into blister fluid, 17-235% penetration into sputum and bronchial secretions, 32-417% penetration into prostatic secretions, 3-146% penetration into CSF, 6-23% penetration into aqueous humour, 28-460% penetration into bone, 94-300% penetration into prostatic tissue, 200-700% penetration into cells; active against Gram negative bacilli (aerobic Gram negative bacilli MIC_{90} 0.25 mg/L; *Aeromonas* (< 5% resistance in Australia), *Bacteroides ureolyticus* (0.06 mg/L), *Bordetella parapertussis* (< 0.06 mg/L), *Bordetella pertussis* (0.12 mg/L), *Brucella melitensis* (0.5-0.8 mg/L), *Burkholderia cepacia, Capnocytophaga* (0.06-0.12 mg/L), *Citrobacter* (most active antibiotic; *Citrobacter diversus* 0.03-0.06 mg/L, *Citrobacter freundii* 0.015-0.25 mg/L), *Enterobacter aerogenes* (98% of hospital isolates), *Enterobacter cloacae* (5% resistant in Australia), *Escherichia coli* (0.3% resistant in Australia), *Haemophilus ducreyi* (< 0.06 mg/L), *Haemophilus influenzae* (0.008-0.03 mg/L), *Haemophilus parainfluenzae* (100% susceptible at 0.06 mg/L), *Haemophilus paraprophilus* (≤ 0.03 mg/L), *Klebsiella oxytoca* (100%), *Klebsiella* pneumoniae (0.5 mg/L), *Legionella* (0.125 mg/L), *Morganella morganii* (0.03 mg/L), various species of *Mycobacterium, Plesiomonas* (< 5% resistance in Australia), indole positive *Proteus*, *Proteus mirabilis* (0.4% resistant in Australia), *Providencia, Pseudomonas aeruginosa, Pseudomonas fluorescens* (0.5-1 mg/L), *Burkholderia pickettii* (0.12-0.25 mg/L), *Pseudomonas stutzeri* (0.5 mg/L), *Rhodococcus* (1 mg/L), *Salmonella* (< 5% resistance in Australia), *Serratia* (*Serratia marcescens* 0.125-1 mg/L), *Shigella* (< 5% resistance in Australia), *Vibrio* (< 5% resistance in Australia), *Wolinella* (≤ 1 mg/L), *Yersinia enterocolitica* (MIC 0.03 mg/L)), some Gram positive cocci (generally rather poor activity against streptococci; *Peptostreptococcus* 0.5 mg/L, coagulase negative staphylococci 0.25-1 mg/L, *Enterococcus avium* 1 mg/L), Gram negative cocci (*Moraxella catarrhalis* 0.03-0.5 mg/L, *Neisseria gonorrhoeae* MIC 0.002-0.03 mg/L (4% less susceptible or resistant in Australia), *Neisseria meningitidis* (< 5% resistance in Australia), *Bacillus* (0.12-1 mg/L), various species of *Mycobacterium* (*Mycobacterium avium-intracellulare*, *Mycobacterium tuberculosis* 0.5-1 mg/L, *Mycobacterium ulcerans* 0.5 mg/L); resistance seen in *Staphylococcus aureus* (12% overall in Australia, 60% in methicillin resistant strains), *Pseudomonas aeruginosa* (13% in Australia), enteric Gram negative bacilli (*Klebsiella pneumoniae* 4% resistant in Australia), *Campylobacter*, poor activity against streptococci, none against anaerobes; constant use can induce resistance; expensive; in WHO model List of Essential Drugs as complementary drug when drugs in main list are known to be ineffective or inappropriate for given individual (tablet)

Indications: should be reserved for treatment of infections resistant to cheaper agents or where an oral agent is desirable and alternatives are parenteral; septic arthritis due to *Mycoplasma hominis*; bacteremia and septicemia due to *Alcaligenes xylosoxidans xylosoxidans, Campylobacter, Acinetobacter*; cat scratch disease; chancroid; cranial parameningeal deep fascial space infections (otogenic, following cranial surgery in normal patient); bacterial dysentery and gastroenteritis in immunocompromised; endocarditis due to *Legionella*; sexually acquired epididymitis and epididymoorchitis; fish spine injury and other water-related infections due to *Vibrio;* bacterial gastroenteritis; gonorrhoea; joint and bone infections; lung abscess; postneonatal pyogenic meningitis due to *Acinetobacter*; meningococcal meningitis prophylaxis; *Mycobacterium avium-intracellulare* infection; pelvic sepsis and pelvic inflammatory disease due to *Neisseria gonorrhoeae*; perichondritis of pinna; pneumonia (due to *Klebsiella pneumoniae*, *Acinetobacter*, severe nosocomial); chronic prostatitis and seminal vesiculitis; *Pseudomonas aeruginosa* pulmonary infection in cystic fibrosis; respiratory tract infections in immunocompromised; *Salmonella* enteric fever (98% cure rate), enterocolitis (86% cure rate), chronic carriage (88% cure rate) and bacteremia/metastatic infection (95% cure rate); local and generalised sepsis, cellulitis and pyoderma, malignant otitis externa due to *Pseudomonas*; *Aeromonas hydrophila* skin infections; acute skin ulcers due to *Flavobacterium meningosepticum*; moderate to severe traveller's diarrhoea; gonococcal vaginitis (β-lactamase positive)

Side Effects: nausea, vomiting, diarrhoea and abdominal pain in up to 10%; anxiety, nervousness, insomnia, euphoria, tremor in 1-4%; seizures reported; possible tendinopathy in adults and arthropathy in children and adults; sunlight sensitivity rash; peripheral neuropathy; red man syndrome with i.v. infusion; *Clostridium* difficile-associated diarrhoea; safety in pregnancy not established; monitor infant for diarrhoea in breastfeeding; dose adjustment required in renal failure and dialysis; antacids, didanosine, H_2-antaganoists, iron and zinc preparations and sucralfate reduce bioavailability; probenecid may reduce urinary excretion; increases theophylline plasma levels and unpredictably enhances warfarin activity; also interacts with caffeine

Norfloxacin: oral fluoroquinolone (take ½ to 1 h before food); no inoculum effect against aerobes, shows inoculum effect against anaerobes; 67% penetration into blister fluid, 90-120% penetration into prostatic tissue, 700-1400% penetration into cells; orally absorbed; spectrum includes *Aeromonas* (100% susceptible), *Bacillus* (1 mg/L), *Bacteroides ureolyticus* (0.25 mg/L), *Bordetella pertussis* (0.25 mg/L), *Citrobacter amalonaticus* (100% susceptible), *Citrobacter diversus* (100% susceptible at ≤ 0.06 mg/L), *Citrobacter freundii* (99% susceptible), *Enterobacter* (0.25 mg/L), Enterobacteriaceae

(0.25-0.5 mg/L), *Haemophilus influenzae* (100% susceptible at 0.12 mg/L), *Haemophilus parainfluenzae* (100% susceptible), *Haemophilus paraprophilus* (0.03 mg/L), *Hafnia alvei* (100% susceptible), *Klebsiella* (0.25 mg/L), *Moraxella* (1mg/L), *Moraxella catarrhalis* (100% susceptible at 0.12 mg/L), *Morganella morganii* (100% susceptible at 0.5 mg/L), *Mycobacterium fortuitum* (0.8 mg/L), *Neisseria gonorrhoeae* (100% susceptible at < 0.12 mg/L), *Neisseria meningitidis* (100% susceptible at < 0.12 mg/L), *Pasteurella multocida* (0.1 mg/L), *Pleisomonas* (0.06-0.5 mg/L), *Proteus mirabilis* (0.4% resistant in Australia), *Proteus vulgaris* (100% susceptible at 0.5 mg/L), *Providencia rettgeri* (0.25 mg/L), *Salmonella* (0.06-0.5 mg/L), *Serratia* (0.5 mg/L), *Shigella* (0.03-0.5 mg/L), coagulase negative staphylococci (100% susceptible at 1 mg/L), *Vibrio parahaemolyticus* (0.5 mg/L), *Yersinia enterocolitica* (0.1-0.5 mg/L); in Australia, *Pseudomonas aeruginosa* 8% resistant, *Enterobacter cloacae* 1% resistant, *Escherichia coli* 0.3% resistant, *Klebsiella pneumoniae* 7% resistant

Indications: urinary tract (acute cystitis, especially complicated infections with mixed infections or with resistant organisms) and gastrointestinal (*Salmonella* enteric fever cure rate 89%, enterocolitis cure rate 80%, chronic carriage cure rate 78%; bacterial dysentery; cholera; bacterial gastroenteritis; moderate to severe traveller's diarrhoea; prophylaxis of traveller's diarrhoea in high risk host) infections; mild epididymitis and epididymoorchitis associated with urinary tract infection; gonorrhoea; less severe acute and chronic prostatitis and seminal vesiculitis

Side Effects: nausea in 3%, headache in 3%, dizziness in 2%, fatigue, rash, abdominal pain, dyspepsia, somnolence, depression, insomnia, constipation, flatulence, heartburn in ≤ 1%, eosinophilia in 2%, elevation of ALT and AST in 2%, increased alkaline phosphatase in 1%, decreased white blood cell or neutrophil count in 1 %; tendinopathy; safety in pregnancy not established; caution in breastfeeding (monitor infant for diarrhoea); dose interval adjustment required in mild to moderate renal failure, not in dialysis; avoid in severe renal failure; antacids, didanosine, H_2-antagonists and sucralfate reduce bioavailability; probenecid may reduce urinary excretion; may increase plasma levels and effects of theophylline and warfarin

Ofloxacin: oral and parenteral fluoroquinolone; 49% penetration into blister fluid, 39-115% penetration into sputum and bronchial secretions, 42-71% penetration into CSF, 2-48% penetration into aqueous humour, 61% penetration into bone, 170-317% penetration into prostatic tissue, 815% penetration into cells; spectrum includes *Acinetobacter calcoaceticus* (100% eradication), *Aeromonas* (100% susceptible at 0.5 mg/L), *Agrobacterium* (MIC 0.5 mg/L), *Bordetella* (100% susceptible at 0.5 mg/L), *Brucella* (0.03 mg/L), *Campylobacter* (100% susceptible at 2 mg/L), *Capnocytophaga* (100% susceptible at 0.5 mg/L), *Chlamydia* (100% susceptible at 2 mg/L, 97% eradication), *Corynebacterium* (100% susceptible at 1 mg/L), *Escherichia coli* (100% susceptible at 2 mg/L, 97% eradication), *Haemophilus ducreyi* (100% susceptible at 2 mg/L), *Haemophilus influenzae* (100% susceptible at 0.12 mg/L, 98% eradication), *Haemophilus parainfluenzae* (100% susceptible at 0.25 mg/L, 100% eradication), *Haemophilus paraprophilus* (0.03 mg/L), *Hafnia alvei* (100% susceptible at 0.25 mg/L), *Klebsiella* (100% susceptible at 1 mg/L, 98% eradication), *Legionella* (100% susceptible at 0.5 mg/L), *Moraxella catarrhalis* (100% susceptible at 0.5 mg/L, 100% eradication), *Morganella morganii* (100% susceptible at 0.5 mg/L), *Mycobacterium fortuitum* (100% susceptible at 2 mg/L), *Mycobacterium kansasii* (100% susceptible at 1 mg/L), *Mycobacterium xenopi* (100% susceptible at 2 mg/L), *Neisseria* (100% susceptible at 0.06 mg/L, 99-100% eradication), *Plesiomonas shigelloides* (0.015 mg/L), *Salmonella* (100% susceptible at 0.12 mg/L), *Shigella* (100% susceptible at 0.5 mg/L), *Staphylococcus aureus* (100% susceptible at 2 mg/L, 93% eradication), coagulase negative staphylococci (100% susceptible at 2 mg/L, 80-97% eradication), *Vibrio* (100% susceptible at 0.5 mg/L), *Yersinia* (100% susceptible at 0.25 mg/L); *Gardnerella vaginalis*, *Listeria*, *Nocardia*, *Mycobacterium avium-intracellulare*, *Mycobacterium chelonae, Mycobacterium scrofulaceum, Bacteroides,* anaerobic Gram positive cocci always resistant

Indications: in Australia, available as eye drops only; bacterial gastroenteritis; pseudomonal osteomyelitis (71% cure rate); prostatitis (85% cure rate); respiratory tract infections (67% cure rate); *Salmonella* enteric fever (100% cure rate), enterocolitis (100% cure rate), chronic carriage (100% cure rate) and bacteremia/metastatic infection (100% cure rate); sexually transmitted infections (81% cure rate); skin infections (81% cure rate); moderate to severe traveller's diarrhoea; urinary tract infection (95% cure rate); conjunctivitis (topical)

Side Effects: tendinopathy, insomnia, headache; *Clostridium* difficile-assocaited diarrhoea; interacts with mineral antacids; dose adjustment required in renal failure and in dialysis; safety in pregnancy not established

Pefloxacin: fluoroquinolone; 59-60% penetration into blister fluid, 83-89% penetration into sputum and bronchial secretions, 9-66% penetration into CSF, 17-42% penetration into aqueous humour, 44-167% penetration into bone, 19-290% penetration into cells; spectrum includes *Acinetobacter* (MIC 1 mg/L), *Aeromonas hydrophila* (0.06 mg/L), *Agrobacterium* (0.25 mg/L), *Bacteroides ureolyticus* (0.12 mg/L), *Campylobacter fetus* (0.125-1 mg/L), *Campylobacter jejuni* (0.125-1 mg/L), *Capnocytophaga* (0.5 mg/L), *Citrobacter diversus* (≤ 0.03-0.5 mg/L), *Citrobacter freundii* (1 mg/L), *Clostridium perfringens* (< 0.25-1 mg/L), *Enterobacter aerogenes* (0.06-0.5 mg/L), *Enterobacter cloacae* (≤ 0.03-1 mg/L), Enterobacteriaceae (0.25-0.5 mg/L), *Escherichia coli* (0.125-0.25 mg/L), *Haemophilus ducreyi* (< 0.06 mg/L), *Haemophilus influenzae* (< 0.015-0.06 mg/L), *Klebsiella oxytoca* (≤ 0.03-0.5 mg/L), *Klebsiella pneumoniae* (0.5 mg/L), *Moraxella catarrhalis* (0.015-0.25 mg/L), *Morganella morganii* (0.5 mg/L), *Mycobacterium tuberculosis* (0.5 mg/L), *Neisseria gonorrhoeae* (0.016 mg/L), *Neisseria meningitidis* (0.03 mg/L), *Plesiomonas shigelloides* (0.06 mg/L), *Proteus mirabilis* (≤ 0.03-1 mg/L), *Proteus vulgaris* (0.25 mg/L), *Providencia* (0.25 mg/L), *Pseudomonas stutzeri* (1 mg/L), *Salmonella* (0.25 mg/L), *Serratia marcescens*

(1 mg/L), *Shigella* (0.06-0.12 mg/L), *Staphylococcus aureus* (0.125-1 mg/L), *Staphylococcus epidermidis* (0.25-1 mg/L), *Staphylococcus haemolyticus* (0.5 mg/L), *Yersinia enterocolitica* (0.25 mg/L)
Indications: myocarditis and pericarditis due to *Yersinia enterocolitica*; *Salmonella* enteric fever (96% cure rate)
Side Effects: tendinopathy; interacts with antacids, cimetidine
ROSOXACIN: fluoroquinolone; spectrum includes *Bordetella pertussis* (MIC 0.025 mg/L), *Enterobacter cloacae* (0.8 mg/L), *Escherichia coli* (0.05 mg/L), *Haemophilus influenzae* (0.05 mg/L), *Klebsiella pneumoniae* (0.8 mg/L), *Neisseria gonorrhoeae* (0.025 mg/L), *Neisseria meningitidis* (< 0.0125 mg/L), *Pasteurella multocida* (0.05 mg/L), *Salmonella typhi* (0.4 mg/L), *Serratia marcescens* (0.4 mg/L), *Shigella dysenteriae* (0.2 mg/L), *Staphylococcus aureus* (0.4 mg/L)
Indications: chancroid
Side Effects: tendinopathy
IRLOXACIN: fluoroquinolone; spectrum includes *Bacillus* (MIC 0.06 mg/L), *Staphylococcus* (0.5 mg/L)
AMIFLOXACIN: fluoroquinolone; spectrum includes *Acinetobacter* (MIC 1 mg/L), *Citrobacter* (0.125-0.5 mg/L), *Corynebacterium jeikeium* (1 mg/L), *Enterobacter* (0.25 mg/L), *Escherichia coli* (0.125 mg/L), *Haemophilus influenzae* (≤ 0.004 mg/L), *Klebsiellla* (1 mg/L), *Proteus* (0.25 mg/L), *Serratia marcescens* (0.5 mg/L), *Staphylococcus haemolyticus* (1 mg/L)
DIFLOXACIN: fluoroquinolone; spectrum includes *Acinetobacter* (MIC 0.12 mg/L), *Bacteroides ureolyticus* (0.5 mg/L), *Citrobacter freundii* (0.5 mg/L), *Citrobacter koseri* (0.12 mg/L), *Enterobacter aerogenes* (0.5 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Legionella* (≤ 0.06-1 mg/L), *Moraxella catarrhalis* (0.12 mg/L), *Neisseria gonorrhoeae* (0.016 mg/L), *Providencia rettgeri* (1 mg/L), *Staphylococcus aureus* (0.25 mg/L), *Staphylococcus epidermidis* (0.5 mg/L)
FLEROXACIN: fluoroquinolone; 62% penetration into blister fluid; spectrum includes *Aeromonas* (MIC ≤ 0.06 mg/L), *Escherichia coli* (< 0.06-1 mg/L), *Haemophilus influenzae* (0.03-0.06 mg/L), *Moraxella catarrhalis* (0.125-0.5 mg/L), *Plesiomonas shigelloides* (≤ 0.06 mg/L), *Salmonella* (0.25-0.5 mg/L), *Shigella* (≤ 0.06-0.125 mg/L), *Staphylococcus aureus* (0.25-0.5 mg/L), *Staphylococcus epidermidis* (0.5-1 mg/L), *Vibrio* (≤ 0.06-0.125 mg/L), *Yersinia frederiksenii* (0.25 mg/L), *Yersinia kristensenii* (≤ 0.06 mg/L), *Yersinia pseudotuberculosis* (0.125 mg/L)
Indications: *Salmonella* enteric fever (cure rate 100%)
Side Effects: tendinopathy; phototoxicity and photocarcinogenicity; interacts with mineral antacids; dose adjustment required in moderate to severe renal failure (glomerular filtration rate < 50 mL/min); dose required after intermittent hemodialysis
LOMEFLOXACIN: spectrum includes aerobic Gram negative bacilli (MIC_{90} 1 mg/L; *Citrobacter* 0.5 mg/L, *Enterobacter* 0.5 mg/L, *Escherichia coli* 0.25 mg/L, *Haemophilus* 0.06 mg/L, *Klebsiella* 1 mg/L, *Morganella morganii* 0.25 mg/L, *Proteus* 0.25 mg/L, *Providencia* 1 mg/L, *Serratia* 0.5 mg/L), coagulase negative staphylococci (1 mg/L), *Neisseria* (0.112 mg/L), *Staphylococcus aureus* (1 mg/L)
Side Effects: phototoxicity and photocarcinogenicity; tendinopathy
LEVOFLOXACIN: optical isomer of ofloxacin; bioavailability 99%, T_{max} 1.3 h, C_{max} 5.1 mg/L, AUC 48 mg.hr/L, protein binding 24-38%, half life 7.6 h; higher activity against ofloxacin sensitive strains and safer; active against *Chlamydophila pneumoniae* (MIC_{90} 0.25 mg/L), *Enterococcus faecalis* (0.5 mg/L), *Escherichia coli* (0.06 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Klebsiella pneumoniae* (0.12 mg/L), *Legionella pneumophila* (0.03 mg/L), *Moraxella catarrhalis* (0.06 mg/L), *Mycoplasma pneumoniae* (0.06 mg/L), methicillin susceptible *Staphylococcus aureus* (0.25 mg/L), *Streptococcus pneumoniae* (1 mg/L)
Indications: uncomplicated urinary tract infections in women, community acquired pneumonia
Side Effects: nausea in 1.3%, diarrhoea in 1%; tendinopathy; *Clostridium difficile*-associated diarrhoea
TOSUFLOXACIN: activity includes *Streptococcus pneumoniae* (MIC 0.39 mg/L, bacterial elimination 90%)
Indications: community-acquired pneumonia
Side Effects: tendinopathy
SPARFLOXACIN: activity includes *Chlamydiophila pneumoniae, Mycoplasma pneumoniae, Streptococcus pneumoniae* (MIC 0.78 mg/L, bacterial elimination 91%)
Indications: community-acquired pneumonia
Side Effects: tendinopathy
GREPAFLOXACIN: high lung tissue concentration, minimal urine concentration; activity includes *Streptococcus pneumoniae* (MIC 0.78 mg/L), *Haemophilus influenzae, Moraxella catarrhalis, Staphylococcus aureus*; withdrawn from market because of severe anaphylaxis, prolongation of QT interval, cardiotoxicity
GATIFLOXACIN: extended spectrum (8-methoxy) oral fluoroquinolone (once daily; timing to food does not matter); bioavailability 96%, T_{max} 1 h, C_{max} 3.8 h, AUC 33 mg.h/L; protein binding 20%, half life 7.8 h; increased activity against Gram positive bacteria (including streptococci), wide activity against Gram negative aerobes, anaerobes and agents of atypical pneumonia; not as active as ciprofloxacin against *Pseudomonas*; active against *Bacteroides fragilis* (MIC_{90} 1 mg/L), *Chlamydophila pneumoniae* (0.06 mg/L), *Clostridium perfringens* (1 mg/l), *Enterococcus faecalis* (0.5 mg/L), *Escherichia coli* (0.06 mg/L), *Fusobacterium nucleatum* (0.5 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Klebsiella pneumoniae* (0.06 mg/L),

Legionella pneumophila (0.016 mg/L), *Mycoplasma pneumoniae* (0.05 mg/L), methicillin susceptible *Staphylococcus aureus* (0.12 mg/L), *Streptococcus pneumoniae* (0.5 mg/L)
Indications: acute sinusitis caused by *Streptococcus penumoniae* or *Haemophilus influenzae;* acute bacterial exacerbation of chronic bronchitis caused by *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenzae* or *Moraxella catarrhalis;* community acquired pneumonia caused by *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenzae, Moraxella catarrhalis, Legionella pneumophila, Chlamydophila pneumoniae* or *Mycoplasma pneumoniae;* urinary tract infections caused by *Escherichia coli, Kelbsiella pneumoniae* or *Proteus mirabilis;* pyelonephritis caused by *Escherichia coli*, uncomplicated skin and skin structure infections
Side Effects: prolongation of QT interval (increased risk with any drug capable of prolonging the QT interval), nausea, diarrhoea, headache, dizziness, tendinopathy, hypoglycaemia, vaginitis in 6%
Trovafloxacin: active against a wide range of respiratory pathogens, especially *Streptococcus pneumoniae* (including penicillin resistant strains); half life ≈ 13 h; suspended in July 1999 because of hypoglycemia, eosinophilia and liver toxicity
Pruifloxacin: fluoroquinolone prodrug; active mainly against Gram negatives (especially *Pseudomonas aeruginosa*)
Indications: may be approved for bronchitis, urinary tract infections, traveller's diarrhoea
Pazufloxacin: similar spectrum to ciprofloxacin
Side Effects: dizziness in 1/2300 only recorded adverse effect; probable tendinopathy
Moxifloxacin: oral (once daily; timing to food does not matter) extended spectrum fluoroquinolone (8-methoxyquinolone); increased activity against Gram positive organisms (including streptococci), wide activity against Gram negative aerobes, anaerobes and agents of atypical pneumonia, but less activity against *Psuedomonas*;; active against *Aeromonas, Bacteroides fragilis* (MIC_{90} 0.5 mg.L), *Bordetella pertussis, Chlamydophila pneumoniae* (0.03 mg/L), *Clostridium perfringens* (0.5 mg/L), *Enterococcus faecalis* (0.5 mg/L), *Escherichia coli* (0.06 mg/L), *Fusobacterium nucleatum* (0.25 mg/L), *Haemophilus influenzae* (0.03 mg/L), *Klebsiella pneumoniae* (0.12 mg/L), *Legionella pneumophila* (0.015 mg/L), *Moraxella catarrhalis* (0.06 mg/L), *Mycobacterium tuberculosis* (0.12-0.5 mg/L), *Mycoplasma pneumoniae* (0.06-0.12 mg/L), *Neisseria gonorrhoeae,* methicillin susceptible *Staphylococcus aureus* (0.12 mg/L), *Streptococcus pneumoniae* (0.12 mg/L)
Indications: acute bacterial sinusitis, acute bacterial exacerbations of chronic bronchitis, community acquired pneumonia
Side Effects: mild to moderate nausea, diarrhoea; prolongation of QT interval (use with caution in patients receiving antiarrhythmia agents—quinidine, procainamide, amiodarone, sotalol); tendinopathy; dose adjustment unnecessary in renal dysfunction or mild to moderate hepatic dysfunction; safety in pregnancy not established
Contraindications: avoid in breastfeeding (insufficient data)
Ansamycins (Rifamycins): active against Gram positive organisms (including staphylococci) and *Mycobacterium*; rapid emergence of resistance dictates usage in combination with unrelated antimicrobials
Side Effects: gastrointestinal effects, orange discolouration of body fluids, staining of soft contact lenses common; allergic reactions, wheeze, flu-like syndrome, blood dyscrasias uncommon; pseudomembranous colitis, neurological symptoms, thrombophlebitis (i.v.) rare
Rifampicin (Rifampin): oral ansamycin (take ½ -1 h before food); inhibits DNA-dependent RNA polymerase; no significant change in V_d or clearance in elderly; bactericidal; lethal for proliferating bacteria and bacteria in latent phase; in high concentrations, penetrates into mammalian cells; active against Gram positive and Gram negative bacteria and mycobacteria; spectrum includes *Bacillus anthracis* (MIC 0.6 mg/L), *Brucella* (0.06-1 mg/L), *Clostridium perfringens* (0.02 mg/L), *Corynebacterium*, *Coxiella burnetii*, *Haemophilus influenzae* (0.02 mg/L), *Legionella* (≤ 0.008-0.5 mg/L), *Listeria monocytogenes* (0.06 mg/L), *Mycobacterium avium* (0.02 mg/L), *Mycobacterium tuberculosis* (0.05 mg/L; spontaneous resistance $1:10^8$ organisms; dosage 600 mg daily or twice weekly), *Neisseria gonorrhoeae* (0.02 mg/L), *Neisseria meningitidis* (< 5% resistance in Australia), *Rickettsia rickettsii*, *Rickettsia typhi*, *Streptococcus canis* (100% susceptible at 0.03 mg/L), *Streptococcus pneumoniae* (0.01 mg/L), *Streptococcus pyogenes* (0.02 mg/L); methicillin resistant *Staphylococcus aureus* 12% resistant in Australia; reduces bacterial adherence, increases neutrophil penetration and intracellular killing; inhibits chemotactic activity of granulocytes; shows microbicidal activity against bacteria ingested by monocytes or macrophages; in WHO Model List of Essential Drugs as antileprosy drug and antituberculosis drug; mode of elimination hepatic, gastrointestinal; very potent inducer of hepatic P450 activity
Indications: mainly tuberculosis, *Mycobacterium avium* complex infections, methicillin resistant *Staphylococcus aureus* infections, prophylaxis in contacts of *Haemophilus influenzae* type b and meningococcal infections; anterior uveitis due to *Mycobacterium tuberculosis*; septic arthritis due to *Mycobacterium tuberculosis*, methicillin resistant *Staphylococcus aureus*, *Brucella*; bacteraemia and septicemia due to methicillin resistant *Staphylococcus aureus* (should never be used alone), *Yersinia enterocolitica*, *Campylobacter fetus* subsp *fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens;* bone marrow infections due to *Mycobacterium tuberculosis*, *Brucella*; tuberculous brain and epidural abscess; brucellosis in non-pregnant/nursing; cat scratch disease; staphylococcal cerebrospinal fluid shunt infections; cholangitis and cholecystitis; chorioretinitis due to *Mycobacterium tuberculosis*; purulent conjunctivitis due to *Haemophilus aegyptius;* treatment and prophylaxis of disseminated mycobacteriosis due to *Mycobacterium gordonae* in non-AIDS patients; endocarditis due to *Brucella*, *Flavobacterium meningosepticum*, *Stenotrophomonas maltophilia*, *Coxiella burnetii*, *Legionella*, methicillin resistant

Staphylococcus aureus; granulomatous synovitis; hepatic granuloma due to *Mycobacterium tuberculosis*; hepatitis due to *Mycobacterium tuberculosis*, *Coxiella burnetii*, *Brucella*; leprosy in adults; lymph gland infections due to *Mycobacterium tuberculosis*; meningitis due to *Flavobacterium meningosepticum*, *Brucella*, *Mycobacterium tuberculosis,* penicillin resistant *Streptococcus pneumoniae*; *Haemophilus influenzae* and meningococcal meningitis carriers and prophylaxis; meningoencephalitis due to *Brucella*; mesenteric lymphadenitis due to *Mycobacterium tuberculosis*; tuberculous mouth ulcers; mycobacteriosis due to *Mycobacterium kansasii*; myocarditis and pericarditis due to *Actinomyces*, *Coxiella burnetii*; oesophagitis due to *Mycobacterium tuberculosis*; ornithosis; otitis media due to *Corynebacterium bovis, Mycobacterium tuberculosis;* peritonitis due to *Mycobacterium tuberculosis*; pneumonia and pneumonitis (tuberculous, moderately severe to severe due to *Legionella pneumophila,* diffuse interstitial due to *Rhodococcus equi*, due to *Mycobacterium szulgai*, *Mycobacterium xenopi*); less severe acute prostatitis and seminal vesiculitis and epididymitis and epididymoorchitis due to *Mycobacterium tuberculosis*; pulmonary abscess; pulmonary tuberculosis due to *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium kansasii*, *Mycobacterium xenopi*, *Mycobacterium szulgai*; acute Q fever; splenic abscess due to *Mycobacterium tuberculosis*; treatment and prophylaxis of tuberculosis; chronic ulcers due to *Mycobacterium marinum, Mycobacterium ulcerans, Arcanobacterium haemolyticum, Corynebacterium bovis*

Side Effects: > 600 mg dose → 'flu syndrome' (fever, chills, headache, bone pain, dizziness); hypersensitivity syndrome (flushing, fever, redness of eyes and thrombocytopenia), shock, shortness of breath, haemolytic anaemia, renal failure, immune thrombocytopenia with high dosage intermittent therapy, hepatotoxicity (in 3% of children; more likely if combined with isoniazid; ≤ 1% of all patients; check liver function before commencing treatment), gastrointestinal disturbances, blurred vision, skin rashes; discolours urine, sputum, tears and sweat (and soft contact lenses) reddish-brown; single case report of hearing loss; dosage modification not required in renal dysfunction nor in dialysis; reduce dosage to ½ to 2/3 normal in liver dysfunction or avoid; accelerates metabolism of several other drugs, including estrogen (high incidence of menstrual irregularities and pregnancy in patients on oral contraceptives); combination with pyrazinamide can cause potentially lethal hepatitis; can significantly reduce plasma concentrations and effects of alfentanil, atovaquone, caspofungin, chloramphenicol, clarithromycin, clozapine, codeine, cortisone, cyclosporin, dapsone, delavirdine, dexamethasone, diazepam, diclofenac, digitoxin, digoxin, diltiazem, disopyramide, efavirenz, fluconazole, fludrocortisone, fluvastatin, glibenclamide, haloperidol, hydrocortisone, itraconazole, ketoconazole (rifampicin levels may increase or decrease), losartan, methadone (producing symptoms of narcotic withdrawal in addicts on maintenance), metoprolol, mexiletine, midazolam, nifedipine, nitrazepam, oral contraceptives (likely to reduce effectiveness), paracetamol, phenytoin, prednisolone, quinidine, tacrolimus, terbinafine, theophylline, tolbutamide (may make diabetic control more difficult), triazolam, verapamil, warfarin (effect may persist 10-14 d after ceasing), human immunodeficiency virus-related protease inhibitors, voriconazole, zidovudine; plasma levels markedly reduced by phenobarbitone and phenytoin; plasma levels may be increased by cotrimoxazole, probenecid; clinically significant interactions also with glucocorticoids, quinidine sulphate, buspirone hydrochloride, zolpidem tartrate, simvastin, propafenone hydrochloride, ondansetron hydrochloride, opiates; increases metabolism of enalapril causing increased plasma levels of active metabolite (enalaprilat); phenobarbitone reduces bioavailability; monitor infant for jaundice if breastfeeding

Contraindications: pregnancy; treatment with protease inhibitors or nonnucleoside transcriptase inhibitors

RIFAMIDE

Indications: biliary infections; treatment and prophylaxis of *Mycobacterium avium* complex infections

Side Effects: hypersensitivity reactions, gastrointestinal disturbances, skin reactions, pain at injection site, yellow discolouration of skin, darkens urine

RIFABUTIN: oral ansamycin (relationship of dose to food doesn't matter)

Indications: treatment and prophylaxis of disseminated mycobacteriosis and pancreatitis due to *Mycobacterium avium-intracellulare;* disseminated mycobacteriosis due to *Mycobacterium malmoense*

Side Effects: rash, hepatitis, fever, thrombocytopenia, orange-coloured body fluids (secretions, urine, tears—may permanently discolour contact lenses); uveitis common; less potent inducer of P450 activity than rifampicin; may reduce plasma levels and effects of clarithromycin, dapsone, diazepam, itraconazole, ketoconazole, methadone, oral contraceptives (likely to reduce effectiveness), oral hypoglycemics, prednisolone, verapamil, warfarin, protease inhibitors (bioavailability of rifabutin increased), nonnucleoside reverse transcriptase inhibitors, digitalis, beta-blockers, anticonvulsives, theophylline; increase of plasma levels by clarithromycin or fluconazole may cause uveitis, severe arthralgias, leucopoenia; significantly decreases bioavailability of indinavir; indinavir increases bioavailability; markedly decreases delavirdine effect (increased metabolism) while increasing rifabutin toxicity (decreased metabolism); dose adjustment not required in renal failure or in dialysis

Contraindications: pregnancy; avoid if breastfeeding (insufficient data); treatment with ritonavir, saquinavir hard-gel cap or delavirdine

RIFAPENTINE: oral ansamycin

Indications: treatment of pulmonary tuberculosis (once weekly dosing effective in continuation phase except in HIV/AIDS patients)

Side Effects: hyperuricemia, elevated ALT and AST, neutropenia; reduces plasma concentrations and increases clearance of indinavir

RIFAXIMIN: broad spectrum, non-absorbable oral ansamycin

Indications: pseudomembranous colitis, small intestinal bacterial overgrowth

SULPHONAMIDES: inhibit dihydropteroate synthetase, thereby producing competitive inhibition of para-aminobenzoic acid; bacteriostatic; mode of elimination renal; decreased bacteriostatic effect under anaerobic conditions

Indications: now have limited use; glanders; hepatitis due to *Burkholderia pseudomallei*, *Mycobacterium leprae*, *Nocardia*; meningitis due to *Nocardia asteroides*; lack of efficacy in treatment of *Shigella* or other intestinal infections

Side Effects: neonatal jaundice (< 2 mo, mother in late pregnancy), hypersensitivity reactions (rare anaphylactic shock), gastrointestinal disturbances (fever, nausea, vomiting, diarrhoea common), skin reactions (rash common), anorexia (common), Stevens-Johnson syndrome (rare), toxic epidermal necrolysis (rare), photosensitivity, headache (uncommon), drowsiness (uncommon), malaise, dizziness, tinnitus, vestibular symptoms, paresthesias, possible crystalluria (depends on solubility and urinary concentration), hematological complications (blood dyscrasias; uncommon), hemolytic anemia in those with glucose-6-phosphate dehydrogenase deficit, megaloblastic anaemia (rare), pulmonary eosinophilia and infiltrates (rare), nephrotoxicity, erythema (rare), hepatitis (rare), aseptic meningitis (rare), ? precipitate polyarteritis nodosa; cause neutropenia by myelosuppression; short-acting safe in therapeutic amounts during pregnancy; further dose required after hemodialysis; likely enhanced warfarin effect (frequent monitoring of prothrombin time essential); very weak association with oral contraceptive failure; unpredictable enhanced warfarin effect

Contraindications: avoid long-acting in renal dysfunction and pregnancy; avoid if breastfeeding G6PD deficient infant or premature infant or < 1 mo

SULPHABENZAMIDE: sulphonamide

SULPHACETAMIDE

Indications: mycobacterial keratitis and iritis

Side Effects: allergy, overgrowth of non-susceptible organisms

Contraindications: pregnancy

SULPHADIAZINE: oral (take with or after food); serum binding 56%; no significant change in protein binding in elderly; in WHO Model List of Essential Drugs

Indications: endocarditis due to *Flavobacterium meningosepticum*; postneonatal pyogenic meningitis due to *Flavobacterium meningosepticum*; nocardiosis; rheumatic fever prophylaxis; tenosynovitis; trachoma

Side Effects: moderate to significant adjustment of dosage in renal failure (rarely, crystalluria, blood dyscrasias)

Contraindications: pregnancy

SILVER SULPHADIAZINE: anti-infective dermatological drug; in WHO Model List of Essential Drugs; staphylococci (including MRSA) and *Pseudomonas aeruginosa* susceptible

Indications: burns prophylaxis; folliculitis and rash due to *Pseudomonas aeruginosa*, *Yersinia*

Side Effects: sensitivity

Contraindications: pregnancy

SULPHADIMIDINE

INDICATIONS: infections with *Nocardia asteroides;* acute maxillary sinusitis; urethritis; lower urinary infections; in WHO Model List of Essential Drugs and in UNHCR Basic List of Essential Drugs

Side Effects: nausea, vomiting, rashes, blood disorders, allergic reactions; take blood counts in prolonged treatment, maintain adequate fluid intake; dose adjustment required in renal failure (monitor for myelosuppression)

Contraindications: pregnancy, children < 6 w, renal/hepatic failure, jaundice, blood disorders; caution in renal impairment, breast feeding

SULPHAMETAPYRAZINE

Indications: trachoma

Side Effects: rashes, dizziness, nausea

Contraindications: liver or kidney disease

SULPHAMETHOXAZOLE: impairs intracellular killing; oral (take with or after food)

Indications: lymphogranuloma venereum; mastoiditis prophylaxis; mycobacteriosis due to *Mycobacterium kansasii*; osteomyelitis and osteochondritis due to *Mycobacterium fortuitum*, *Nocardia asteroides*; mycobacterial local and generalised sepsis

Side Effects: moderate to significant adjustment of dosage in renal failure (rarely, crystalluria, blood dyscrasias (monitor for myelosuppression)) and in dialysis; toxic level > 450 μmol/L

Contraindications: pregnancy

SULPHATHIAZOLE: sulphonamide

SULPHIDOXIME: sulphonamide

SULPHISOXAZOLE: delayed absorption, no significant change in V_d, reduced clearance in elderly

Indications: chancroid; *Mycobacterium chelonae* and *Mycobacterium fortuitum* infections; nocardiosis; otitis media prophylaxis; trachoma
Side Effects: rashes, dizziness, nausea, aseptic meningitis
Contraindications: liver or kidney disease; pregnancy
SULPHAMETHIZOLE: only readily accessible oral straight sulphonamide on market in Australia
Indications: urinary tract infections
Side Effects: infrequent nausea, vomiting, abdominal pain, anorexia, pancreatitis, malaise, headache, dizziness, fever, rare hypersensitivity, aseptic meningitis, extremely rare serious blood dyscrasias; moderate to significant adjustment of dosage in renal failure (rarely, crystalluria, blood dyscrasias)
Contraindications: last month of pregnancy, lactation
TRIPLE SULPHA
Indications: cellulitis due to *Mycobacterium fortuitum*; pulmonary tuberculosis due to *Mycobacterium chelonae, Mycobacterium fortuitum;* bacterial vaginitis (topical)
TRIMETHOPRIM: inhibits enzyme dihydrofolate reductase; bacteriostatic; oral (take with or after food; daily dose); serum protein binding 50%; requires further dose after haemodialysis; impairs intracellular killing; spectrum includes *Haemophilus influenzae* (MIC 0.5 mg/L), *Listeria monocytogenes* (0.12 mg/L); *Moraxella catarrhalis* 98% intrinsic resistance (possibly all resistant in clinical practice), *Pseudomonas aeruginosa* 100% intrinsic resistance; in Australia, *Streptococcus pneumoniae* 52% resistant, *Escherichia coli* 22% resistant, *Enterobacter cloacae* 23% resistant, *Klebsiella pneumoniae* 26% resistant, *Proteus mirabilis* 28% resistant, *Staphylococcus aureus* 27% resistant overall (methicillin susceptible strains 3%); in WHO Model List of Essential Drugs as complementary drug for use when drugs in main list are known to be ineffective or inappropriate for a given individual; mode of elimination renal
Indications: acute cystitis treatment and prophylaxis of recurrent; prophylaxis of recurrent nonvenereal dysuria-frequency syndrome; mild acute epididymitis and epididymoorchitis associated with urinary tract infection; listerial meningitis; less severe acute and chronic prostatitis and seminal vesiculitis; mild acute pyelonephritis; prophylaxis of traveller's diarrhoea in high risk children
Side Effects: rash in 8%, sore mouth, aseptic meningitis, others as for sulphonamides but less common gastrointestinal and hamatological effects; no adjustment of dosage in renal failure but monitor for blood dyscrasias; dose required after intermittent hemodialysis; safety in pregnancy not established; safe in breastfeeding; additional suppression of folate metabolism with pyrimethamine may result in megaloblastic anaemia, serious pancytopenia; less likely enhanced warfarin effect; increases plasma levels of digoxin, phenytoin; weak association with oral contraceptive failure
COTRIMOXAZOLE: trimethoprim + sulphamethoxazole; inhibits sequential steps in folic acid synthesis, preventing DNA replication; bactericidal; well absorbed; wide tissue and CNS distribution; oral (twice a day, with or after food); optimum degree of antibacterial synergy may be lost with extremes of urinary pH (particularly acid pH); renally eliminated; spectrum includes *Aeromonas hydrophila* (100% susceptible), *Alcaligenes*, *Brucella* (≤ 0.25-1 mg/L), *Citrobacter diversus* (88% susceptible), *Eikenella corrodens* (95% susceptible), *Enterobacter aerogenes* (98% of hospital isolates), *Enterobacter cloacae* (12% resistant in Australia), *Enterococcus durans* (100% susceptible at 1 mg/L), *Enterococcus faecalis* (100% susceptible at 1 mg/L), *Enterococcus faecium* (100% susceptible at ≤ 0.06 mg/L), *Flavobacterium*, *Haemophilus influenzae* (not meningitis; 0.03-0.25 mg/L), *Haemophilus parainfluenzae*, *Haemophilus paraprophilus* (0.03-1 mg/L), *Klebsiella oxytoca* (100%), *Listeria monocytogenes* (100% susceptible at ≤ 0.06 mg/L; drug of choice), *Moraxella catarrhalis* (7% resistant in Australia), *Morganella morganii* (100% susceptible at 1 mg/L), *Neisseria gonorrhoeae*, *Neisseria meningitidis* (≤ 0.06-0.6 mg/L), *Nocardia* (drug of choice), *Pasteurella multocida* (95% susceptible), *Proteus mirabilis* (18% resistant in Australia), *Proteus vulgaris* (100% susceptible at 0.5 mg/L), *Pseudomonas pseudomallei*, *Salmonella* (100% susceptible), *Serratia* (88% susceptible), *Shigella* (100% susceptible), *Staphylococcus aureus* (26% resistance (mainly in methicillin resistant strains) in Australia), *Stenotrophomonas maltophilia* (98% of hospital isolates), *Streptococcus agalactiae* (0.12-0.25 mg/L), *Streptococcus equinus* (100% susceptible at 0.5 mg/L), *Streptococcus pneumoniae* (80% resistant in Australia), *Yersinia*; *Streptococcus pyogenes* resistant; *Pseudomonas aeruginosa* 100% intrinsic resistance; in Australia, *Escherichia coli* 19% resistant, *Klebsiella pneumoniae* 15% resistant; in WHO Model List of Essential Drugs; cheap
Indications: widespread use as broad spectrum agent, particularly in respiratory and urinary tract infections; should be restricted to few clinical situations where it is drug of choice (cat and dog bite infections; human bite and clenched fist infections; *Listeria monocytogenes* infection in penicillin hypersensitive; *Nocardia* infections; acute otitis media in remote areas); also used for reactive arthritis due to *Shigella*, *Salmonella*, *Yersinia*; bacteraemia and septicemia due to *Salmonella*, *Burkholderia pseudomallei*, *Alcaligenes xylosoxidans, Yersinia enterocolitica, Campylobacter fetus subsp fetus, Methylobacterium extorquens, Agrobacterium tumefaciens, Stenotrophomonas maltophilia, Ochrobacterium anthropi, Oerskovia;* asymptomatic bacteriuria; bone marrow infection due to *Brucella*, *Salmonella typhi;* brain and epidural abscess due to *Brucella*; brucellosis in children < 8 y; cerebrospinal fluid shunt infections due to *Staphylococcus*, diphtheroids, *Propionibacterium*; cellulitis due to *Mycobacterium fortuitum*; chancroid; cholera; acute cystitis in children when trimethoprim syrup not available; disseminated mycobacteriosis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*; bacterial

dysentery; dysuria-frequency syndrome due to Gram negative bacilli; endocarditis due to *Brucella*, *Stenotrophomonas maltophilia*, *Coxiella burnetii;* enteric fevers; acute epididymitis and epidiymoorchitis due to *Salmonella*; erysipelas-like condition due to *Yersinia enterocolitica*; glanders; gonorrhoea; granuloma inguinale; bacterial hepatic abscess; hepatic granuloma due to *Burkholderia pseudomallei*; hepatitis due to *Salmonella typhi*, *Shigella, Burkholderia pseudomallei, Brucella, Yersinia pseudotuberculosis;* melioidosis; meningoencephalitis due to *Brucella*; mesenteric lymphadenitis due to *Yersinia*; mycetoma due to nocardiforms; orchitis due to *Salmonella*; osteomyelitis; otitis media due to *Haemophilus influenzae*, *Neisseria;* peritonitis due to *Mycobacterium chelonae, Mycobacterium fortuitum;* pharyngitis; pneumonia (mild *Haemophilus influenzae*, *Stenotrophomonas maltophilia*, *Acinetobacter*); *Burkholderia pseudomallei* pneumonitis; pseudotuberculosis; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; pulmonary tuberculosis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*; less severe acute prostatitis; prostatic abscess; acute respiratory infection in outpatients; rhinoscleroma; rickettsioses; acute sinusitis; systemic infection prophylaxis in agammaglobulinemia, cell-mediated immunity disorders, granulocytopenia, microbial abnormality; tenosynovitis; moderate to severe traveller's diarrhoea; traveller's diarrhoea prophylaxis in high risk host; severe lower urinary tract infections; whooping cough, treatment of community-associated methicillin resistant *Staphylococcus aureus*

Side Effects: very high risk of serious adverse reactions (similar to sulphonamides), low risk of gastrointestinal adverse effects, moderate risk of skin rash; nausea and vomiting (7% in AIDS), skin reactions (10% in AIDS), headache, dizziness, haematological complications (folate metabolism may be impaired, especially in elderly; neutropenia 17% in AIDS; thrombocytopenia), pseudomembranous colitis, hypersensitivity reactions common, bone marrow suppression, megaloblastic marrow, azotemia, hepatitis, elevated levels of liver enzymes (20% in AIDS); nephrotoxicity, potential false increase in serum creatinine, hypoglycaemia in renal insufficiency (adjust dose appropriately, monitor renal function); acute hypotensive syndrome resembling septic shock in AIDS; may cause photosensitivity, hearing loss; hyperkalemia; possible additive antifolate effect with methotrexate, causing bone marrow depression, pancytopenia; aseptic meningitis; toxic level > 150 mg/L peak sulphamethoxazole, > 3 mg/L peak trimethoprim (monitor occasionally in renal impairment or with high doses); dose adjustment required in renal failure and in dialysis; take blood counts in prolonged treatment and in renal failure; maintain adequate fluid intake; minor inhibitor of CYP enzymes; decreases cyclosporin levels; potentiation of effect of warfarin likely by inhibiting metabolism; serious pancytopenia and megaloblastic anaemia from additional suppression of folate metabolism with pyrimethamine; plasma levels of rifampicin may be increased; weak association with oral contraceptive failure

Contraindications: pregnancy, children < 6 w, renal/hepatic failure, breast feeding (infant premature or < 1 mo); avoid in elderly

NIBRISIN: trimethoprim + sulphadiazine

Indications: bronchitis; pneumonia; sinusitis; tonsillitis

AMINOGLYCOSIDES: parenteral; act on 30S ribosome producing nonsense proteins from misreading of mRNA; bactericidal; activity depends on concentrations achieved over time; once-daily dosing as efficacious, cheaper and less likely to cause nephrotoxicity than more frequent dosing; *Stenotrophomonas maltophilia* 79% intrinsic resistance (possibly all resistant in clinical practice), anaerobes 100% intrinsic resistance, *Enterococcus* and *Streptococcus* 100% intrinsic resistance; induce postantibiotic effect even after brief periods of exposure; decreased antibacterial effect under anaerobic conditions; mode of elimination renal; decrease neutrophil chemotaxis, no effect on phagocytosis, reduce bacterial adherence, no effect on neutrophil penetration, decrease intracellular killing; no effective CNS penetration; produce relatively low amounts of endotoxins

Indications: cellulitis due to *Aeromonas hydrophila*; purulent conjunctivitis due to *Pseudomonas aeruginosa*; endocarditis due to *Escherichia coli*, *Corynebacterium*; infantile diarrhoea; infections with coliforms; intraabdominal infections; neonatal necrotising enterocolitis; bacterial parotitis and submandibular sialadenitis; initial treatment of serious Gram negative infections; systemic infections in granulocyptopenia

Side Effects: neurotoxicity (common), gastrointestinal disturbances, skin reactions (sensitivity with topical use), neuromuscular blockade (rare respiratory depression; administer calcium and neostigmine for severe; increases effect of neuromuscular blockers and potentiates respiratory depression), nephrotoxicity (common; enhanced by aciclovir, amphotericin, cephalothin, bumetanide, ethacrynic acid, frusemide, vancomycin, NSAIDS, cyclosporin, cidofovir, capreomycin; prevented by polyaspartic acid), ototoxicity (vestibular and auditory; common; increased risk when combined with 'loop' diuretics (bumetanide, ethacrynic acid, frusemide), capreomycin), hypersensitivity (uncommon); inactivation by penicillins in renal insufficiency or if mixed together; relative contraindications: hearing impairment, old age, neuromuscular blockade, previous aminoglycoside exposure; increase nephrotoxicity of cyclosporine; in renal insufficiency, monitor renal function, avoid prolonged therapy and concurrent cephalothin (increased risk of nephrotoxicity, particularly in elderly), avoid other ototoxic drugs and neuromuscular blocking agents (potentiate respiratory suppression produced by these agents), avoid neomycin; further dose required after hemodialysis

AMIKACIN: aminoglycoside most resistant to enzymatic inactivation; at least 20 times as expensive as gentamicin; no significant change in clearance in elderly; low to moderate postantibiotic effect; no inoculum effect; spectrum includes

Aeromonas hydrophila (100% susceptible), Enterobacteriaceae (< 5% resistance in Australia), *Mycobacterium chelonae*, *Yersinia enterocolitica* (100% susceptible); in Australia, *Pseudomonas aeruginosa* 13% resistant; enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may occur by production of 6′-aminoglycoside acetyltransferase/2″-aminoglycoside phosphotransferase, 6′-aminoglycoside acetyltransferase or 3′-aminoglycoside phosphotransferase

Indications: must be reserved for treating infections due to microorganisms resistant to other aminoglycosides; bacteraemia and septicemia due to *Pseudomonas aeruginosa*; disseminated mycobacteriosis due to *Mycobacterium avium* in AIDS, *Mycobacterium chelonae* and *Mycobacterium fortuitum* in non-AIDS patients; endocarditis due to *Pseudomonas aeruginosa*, *Mycobacterium chelonae*, *Mycobacterium fortuitum*; meningitis due to *Pseudomonas aeruginosa*, *Nocardia asteroides*; mycetoma due to nocardiforms; mycobacteriosis due to *Mycobacterium kansasii*; peritonitis due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*; *Klebsiella pneumoniae* pneumonia; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; mycobacterial local and generalised sepsis

Side Effects: less nephrotoxic than gentamicin or sisomicin but more audiotoxic than netilmicin; toxic level > 5 mg/L trough (monitor routinely at least once during a course of therapy); dose adjustment needed for renal failure and dialysis

Contraindications: pregnancy

FRAMYCETIN (SOFRAMYCIN): aminoglycoside

Indications: *Staphylococcus aureus* blepharitis (ointment); 'swimmer's ear' (topical); chronic discharging otitis media in remote communities

Side Effects: ototoxicity (cochlear function), intestinal malabsorption (continued use of oral)

Contraindications: use in ear when drum perforation known or suspected; pregnancy

GENTAMICIN: aminoglycoside of choice for most cases (≥ 95%) of hospital acquired aerobic Gram negative sepsis but more nephrotoxic than amikacin or tobramycin; cheaper than kanamycin; i.m. or i.v. twice daily or once daily (adults only) or single i.m. dose (urinary tract infection in children); 27% bronchial penetration 2-3 h after 0.2 mg/kg i.m. dose; 25-30% serum protein binding; no significant change in V_d in elderly; low to moderate postantibiotic effect; bactericidal; lethal for proliferating bacteria and for bacteria in latent phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; active against Gram positive and Gram negative bacteria—wide spectrum including *Aeromonas hydrophila* (100% susceptible), *Bacillus* (100% susceptible), *Brucella* (100% susceptible), *Campylobacter jejuni* (100% susceptible), *Citrobacter diversus* (100%), *Enterobacter aerogenes* (98% of hospital isolates), *Enterobacter cloacae* (14% resistant in Australia), *Escherichia coli* (0.9% resistant in Australia), *Hafnia alvei, Helicobacter pylori*, *Klebsiella oxytoca* (98% of hospital isolates), *Listeria monocytogenes* (0.5-1 mg/L), *Morganella morganii* (100%), *Neisseria gonorrhoeae* (1 mg/L), *Proteus mirabilis* (2% resistant in Australia), *Pseudomonas fluorescens* (≤ 0.03-1 mg/L), *Pseudomonas putida* (≤ 0.03-1 mg/L), *Pseudomonas putrefaciens* (0.13-0.5 mg/L), *Pseudomonas stutzeri* (0.13-1 mg/L), *Sarcina lutea* (100% susceptible), *Serratia marcescens* (100%), *Staphylococcus aureus* (0.5 mg/L); in Australia, *Pseudomonas aeruginosa* 17% resistant, *Klebsiella pneumoniae* 11% resistant; enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may occur by production of 6′-aminoglycoside acetyltransferase/2″-aminoglycoside phosphotransferase (in Australia, *Enterococcus faecalis* 12% high level resistance, *Enterococcus faecium* 29% high level resistance); shows inoculum effect; in WHO Model List of Essential Drugs as drug requiring specific expertise, diagnostic precision, individualisation of dosage or special equipment for proper use, and for which adverse effects diminish benefit/risk ratio (indiscriminate use must be discouraged and dosage always calculated according to weight and renal clearance of patient)

Indications: after other antibiotics have failed; *Aeromonas hydrophila* infections; septic arthritis (hospital acquired, due to coliforms, *Pseudomonas aeruginosa*, *Serratia marcescens*); bacteremia and septicemia (infection from female genital tract, focus probably biliary or gastrointestinal tract, focus probably urinary tract, focus probably decubitus or ischaemic ulcer or diabetic foot ulcer, focus probably intravascular catheter, unidentified source in adult or remote area, febrile neutropenic patient with no renal impairment/not on nephrotoxic drugs and *Pseudomonas aeruginosa* suspected, neonatal, due to *Shigella*, *Pseudomonas aeruginosa*, *Acinetobacter*, *Enterococcus*, *Yersinia enterocolitica*, *Campylobacter fetus* subsp *fetus*, *Methylobacterium extorquens*, *Agrobacterium tumefaciens*); brain and epidural abscess from ear and mastoid or due to *Haemophilus*; brucellosis; burn infections; cerebrospinal fluid shunt infections due to *Enterococcus*, *Streptococcus*, aerobic Gram negative bacilli; cholangitis and cholecystitis; compound fracture prophylaxis if wound soiling or severe tissue damage and/or devitalised tissue; acute cystitis in children; endocarditis prophylaxis (dental procedures or upper respiratory tract interventions in high risk patients) and treatment; endometritis; endophthalmitis; severe acute epididymitis and epididymoorchitis associated with urinary tract infection or due to *Pseudomonas aeruginosa*; penetrating eye injuries; folliculitis associated with spa; severe *Yersinia enterocolitica* gastroenteritis; granuloma inguinale; hepatic abscess; meningitis due to *Campylobacter fetus* subsp *fetus*; mycotic aneurism; nasal septal abscess; necrotising fasciitis; neonatal sepsis; osteomyelitis and osteochondritis (acute neonatal, due to *Aeromonas*); otitis media due to *Pseudomonas aeruginosa*, enteric Gram negative bacilli); pancreatic abscess; panophthalmitis due to *Pseudomonas aeruginosa*; parametritis; pelvic sepsis and pelvic inflammatory disease related to trauma; perinatal generalised disease due to penicillinase-producing *Neisseria gonorrhoeae*, coliforms; peritonitis (suspected bowel origin, spontaneous); pneumonia (intensive care; moderate nosocomial with

no specific risk factors; severe community acquired; due to Gram negative bacilli, especially *Klebsiella pneumoniae*, *Acinetobacter*); severe acute prostatitis and seminal vesiculitis; *Pseudomonas aeruginosa* infections; severe acute pyelonephritis; salpingitis; local and generalised sepsis (including *Enterococcus*, *Aeromonas*); localised skin lesions due to Gram negative bacilli; surgical prophylaxis (cardiovascular; vascular graft; breast; dialysis access; gastrointestinal; colorectal; appendicectomy; urinary tract; implant; perforated or gangrenous viscus; muscular, skeletal and soft tissue trauma; ophthalmic; joint; endoscopic procedures); symbiotic gangrene; staphylococcal toxic shock syndrome; tubo-ovarian abscess; catheter-associated urinary tract infection; vascular graft infection; water-related infections

Side Effects: headache, ototoxicity (mainly vestibular function), reversible nephrotoxicity, photosensitivity, Stevens-Johnson syndrome, vasculitis; causes neutropenia by myelosuppression; in renal insufficiency, contraindicated or dosage adjustment necessary; dose adjustment required in dialysis; toxic level > 2 mg/L trough (monitor routinely at least once during a course of therapy); incompatible with ampicillin, carbenicillin, heparin, cephalothin, colistimethate

Contraindications: pregnancy; caution in renal impairment

KANAMYCIN: aminoglycoside; not as active as, and more expensive than, gentamicin; may show inoculum effect; spectrum includes *Moraxella* (MIC ≤ 0.03-1 mg/L), *Mycobacterium* (dosage 0.5-1 mg daily); enterococcal resistance, resulting in loss of synergy with cell wall active antibacterials, may occur by production of 6′-aminoglycoside acetyltransferase/2″-aminoglycoside phosphotransferase, 6′-aminoglycoside acetyltransferase or 3′-aminoglycoside phosphotransferase

Indications: none

Side Effects: systemic hypersensitivity reactions, paresthesias, headache, ototoxicity (mainly cochlear), pain at injection site, renal toxicity; maximum permissible blood level 20 mg/L; incompatible with ampicillin, cephalothin, heparin, lincomycin, methicillin, novobiocin

NEOMYCIN: aminoglycoside; bactericidal; active against bacteria irrespective of growth phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; active against Gram positive and Gram negative bacteria and mycobacteria; spectrum includes *Klebsiella* (MIC 1 mg/L), *Moraxella* (0.5 mg/L), *Neisseria gonorrhoeae* (1 mg/L)

Indications: cholera carriers (oral); purulent conjunctivitis (topical); staphylococcal enterocolitis (oral); otitis media prophylaxis (topical); panophthalmitis due to *Pseudomonas aeruginosa* (topical); 'swimmer's ear' (topical); no proven value in the treatment of diarrhoea, associated with gastrointestinal toxicity and may prolong or exacerbate diarrhoea, promotes resistance to antimicrobial agents

Side Effects: most nephrotoxic and ototoxic (mainly cochlear function) of aminoglycosides, intestinal malabsorption with continued use of oral preparations, rashes (fixed drug reaction, Stevens-Johnson syndrome); less likely enhanced warfarin effect; topical use may induce sensitisation

Contraindications: avoid in renal dysfunction; pregnancy

NEOMYCIN + BACITRACIN: anti-infective dermatological drug; in WHO Model List of Essential Drugs

Indications: bacterial skin infections

Side Effects: high risk of skin allergy (no improvement suggests allergy to drug)

NETILMICIN: aminoglycoside; more resistant to inactivating enzyme than gentamicin and tobramycin but less resistant than amikacin; as expensive as tobramycin; spectrum includes *Moraxella* (MIC ≤ 0.03-0.5 mg/L), *Shewenella putrefaciens* (0.25-0.5 mg/L), *Pseudomonas stutzeri* (0.06-1 mg/l), *Streptococcus canis* (1 mg/L); enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may occur by production of 6′-aminoglycoside acetyltransferase/2″-aminoglycoside phosphotransferase or 6′-aminoglycoside acetyltransferase

Indications: endocarditis due to *Enterococcus*, *Streptococcus equinus* and other relatively resistant streptococci, *Neisseria mucosa, Rothia dentocariosa* in elderly

Side Effects: less ototoxic and nephrotoxic than gentamicin and tobramycin but more auditoxic than amikacin; adjustment required in renal failure and in dialysis

Contraindications: pregnancy

SISOMYCIN: most active aminoglycoside in vitro against majority of Enterobacteriaceae; more efficacious in vivo than tobramycin but more nephrotoxic than amikacin; spectrum includes *Moraxella* (MIC ≤ 0.03-0.25 mg/L), *Pseudomonas fluorescens* (0.06-0.5 mg/L), *Pseudomonas putida* (0.06-0.5 mg/L), *Shewenella putrefaciens* (0.13-0.5 mg/L), *Pseudomonas stutzeri* (0.06-0.5 mg/L)

STREPTOMYCIN: aminoglycoside; acts on initiation, codon recognition and translocation; bactericidal; active against bacteria irrespective of growth phase; in high concentrations, penetrates into mammalian cells; active against Gram positive and Gram negative bacteria and mycobacteria; enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may result from production of streptomycin adenyltransferase or ribosomally; 25-30% protein binding; in WHO Model List of Essential Drugs as antituberculous drug and in UNHCR Specialised List of Essential Drugs

Indications: use now limited to occasional selected cases of tuberculosis, other mycobacterial infections and enterococcal endocarditis (not registered for use in Australia)

Side Effects: systemic hypersensitivity reactions, peripheral neuropathy, ototoxicity (mainly vestibular function; hearing and balance problems), pain at injection site, blood dyscrasias, visual disturbances, nephrotoxicity, erythema nodosum, fixed

drug reaction, lupus erythematosus, photosensitivity, pustulosis, Stevens-Johnson syndrome, vasculitis; causes neutropenia by myelosuppression; maximum permissible blood level 20 mg/L; incompatible with carbenicillin, erythromycin, heparin, novobiocin

Contraindications: pregnancy; avoid in breastfeeding (insufficient data); in renal insufficiency, contraindicated or dosage adjustments necessary

TOBRAMYCIN: aminoglycoside; i.v. and nebulised; once daily administration feasible; marginally more active than gentamicin against *Pseudomonas aeruginosa* (but not other Gram negative bacteria) in vitro but several times as expensive; not as efficacious in vivo as sisomicin; spectrum includes *Aeromonas hydrophila* (100% susceptible), *Citrobacter koseri* (100%), *Enterobacter aerogenes* (100%), *Enterobacter cloacae* (95% of hospital isolates), *Escherichia coli* (99% of hospital isolates), *Hafnia alvei* (100% susceptible), *Klebsiella oxytoca* (100%), *Morganella morganii* (100%), *Neisseria gonorrhoeae* (MIC 0.5 mg/L), *Proteus mirabilis* (97% of hospital isolates), *Proteus vulgaris* (100%), *Providencia*, *Pseudomonas aeruginosa* (5% resistant in Australia), *Pseudomonas stutzeri* (0.13-1 mg/L), *Staphylococcus aureus* (0.25 mg/L); in Australia, *Klebsiella pneumoniae* 6% resistant; enterococcal resistance, resulting in loss of synergism with cell wall active antibacterials, may result from production of 6′-aminoglycoside acetyltransferase/2″-aminolgycoside phosphotransferase or 6′-aminoglycoside acetyltransferase; no significant change in V_d in elderly; low to high postantibiotic effect

Indications: pseudomonal infections in cystic fibrosis patients; may have a role in treatment of suspected or proven *Pseudomonas* septic arthritis, bacteremia and septicemia, purulent conjunctivitis (topical), acute cystitis, meningitis, myocarditis and pericarditis, osteomyelitis and osteochondritis, pneumonia, sepsis; septic arthritis due to coliforms, *Serratia marcescens*; bacteremia and septicemia (focus probably urinary tract, febrile neutropenic patient with no renal impairment/not on nephrotoxic drugs and *Pseudomonas aeruginosa* suspected); cranial parameningeal deep fascial space infections following cranial surgery in normal patient; endocarditis due to Gam negative bacilli; emphysematous gastritis; keratitis and iritis due to Gram negative bacilli; myocarditis and pericarditis due to *Yersinia enterocolitica*; malignant otitis externa due to *Pseudomonas aeruginosa*; perianal and perirectal abscess and cellulitis in patients with malignant disease; peritonitis; pneumonia due to *Corynebacterium pseudodiphtheriticum*

Side Effects: less nephrotoxic than gentamicin but more nephrotoxic and audiotoxic than netilmicin (no ototoxicity or nephrotoxicity with nebulised form); muscle twitches, hypomagnesia, hypersensitivity syndrome; moderate to significant adjustment of dosage in renal failure (otoxicity, nephrotoxicity; serum levels must be monitored (toxic level > 2 mg/L)); dose adjustment required in dialysis; safe in breastfeeding

Contraindications: pregnancy

SPECTINOMYCIN: aminocyclotol; in WHO Model List of Essential Drugs as drug with limited indications or narrow spectrum of activity; mode of elimination renal

Indications: active against a wide range of bacteria but clinical use restricted to treatment of uncomplicated gonorrhoea (ß-lactamase positive; resistance not yet reported in Australia), chancroid, rape prophylaxis

Side Effects: gastrointestinal disturbances, skin reactions, pain at injection site, hypersensitivity syndrome; use single dose only in renal dysfunction and in dialysis; probably safe in pregnancy

Contraindications: avoid if breastfeeding (insufficient data)

CHLORAMPHENICOL: oral (take ½ - 1 h before food) and parenteral; acts on 50S ribosome to inhibit peptide bonding, acts on transpeptidation and translocation; low postantibiotic effect; bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; penetrates well into mammalian cells; active against Gram positive and Gram negative bacteria; spectrum includes *Actinomyces* (good activity; 98-100% susceptible), anaerobic cocci (98-100% susceptible), *Arachnia* (98-100% susceptible), *Bacteroides* (100% susceptible), *Brucella*, *Chlamydia, Clostridium* (good activity; 100% susceptible), *Eubacterium* (good activity), *Fusobacterium* (good activity; 100% susceptible), *Haemophilus influenzae* (3% resistant in Australia), *Listeria*, *Moraxella catarrhalis* (MIC 0.25-0.5 mg/L), *Neisseria meningitidis* (< 5% resistance in Australia), *Rickettsia canada*, *Rickettsia rickettsii, Rickettsia tsutsugamushi, Rickettsia typhi, Salmonella*; in Australia, *Streptococcus pneumoniae*; no effect on opsonisation, reduces neutrophil chemotaxis, no effect on phagocytosis, no effect on capsule enzyme/toxin, increases neutrophil penetration, reduces intracellular killing; shows microbicidal activity against bacteria ingested by monocytes or macrophages; may show inoculum effect; in WHO Model List of Essential Drugs as drug for which adverse effects diminish benefit/risk ratio (oily suspension in complementary list for use in epidemics of meningococcal meningitis when the scale of the epidemic precludes any other form of therapy); mode of elimination hepatic and renal

Indications: potent, potentially toxic, broad spectrum antibiotic reserved for life-threatening situations; clostridial abortional and puerperal infections; septic arthritis due to *Haemophilus influenzae*, *Eikenella corrodens*, *Salmonella*; brain abscess; bacteraemia and septicemia (infection from respiratory tract in children, due to *Salmonella*); bacterial blepharitis (topical); bone marrow infection due to *Salmonella typhi*; brain abscess; cellulitis due to anaerobes, *Haemophilus influenzae*;; cranial parameningeal deep fascial space infections (otogenic, rhinogenic, odontogenic in normal patient); dental infections; acute and chronic empyema; ear infections; enteric fever; acute epiglottitis in normal host; granuloma inguinale; hepatic abscess due to *Chromobacterium violaceum*; hepatic granuloma due to *Salmonella*; hepatitis due to *Salmonella typhi*,

Rickettsia; intraabdominal abscess; mastoiditis (treatment failure); intracranial bacterial infections; intraocular infections; post-neonatal pyogenic meningitis; myocarditis and pericarditis due to *Actinomyces*, *Actinobacillus actinomycetemcomitans*, *Rickettsia rickettsii*; anaerobic osteomyelitis and osteochondritis; perinatal generalised disease due to coliforms; peritonitis; pertussis; pneumonia (*Chromobacterium violaceum*, other Gram negatives, intensive care); pneumonitis due to *Pseudomonas pseudomallei*; pulmonary gangrene; acute Q fever; louse-borne relapsing fever; acute respiratory infections in hospitalised patient; rickettsial haemorrhagic fever; rickettsioses; Rocky Mountain spotted fever; rickettsial localised skin lesions; acute skin ulcers due to *Chromobacterium violaceum*; splenic abscess due to *Salmonella*, *Escherichia coli*; ophthalmic surgery prophylaxis (topical); typhoid; endemic, epidemic and scrub typhus

Side Effects: headache, nausea, vomiting, hematological complications (leucopoenia (neutropenia), thrombocytopenia, reversible dose-dependent bone marrow hypoplasia) common; stomatitis, glossitis, nausea, vomiting, diarrhoea, enterocolitis, pseudomembranous colitis, confusion, skin reactions (pemphigus, cutaneous porphyria, pustulosis, Stevens-Johnson syndrome, vasculitis) uncommon; rare (1 in 30,000 courses) irreversible dose-independent aplasia; possible increased risk with cimetidine), hyperbilirubinemia in newborn, circulatory collapse (grey baby syndrome) in newborn, optic neuritis, superinfection, hearing loss, anaphylaxis, neuropathy; toxic level 20 mg/L peak (monitor routinely in newborn); dosage modification not required in renal dysfunction but monitor peripheral blood count (marrow suppression); further dose not required after hemodialysis; reduce dose to ½ - 1/3 in liver dysfunction; avoid repeated courses and prolonged treatment; periodic blood counts required; may increase plasma levels and effects of oral hypoglycemics, phenytoin and warfarin (likely enhanced effect); plasma levels decreased to subtherapeutic amounts by enzyme-inducing agents (eg., anticonvulsants, phenobarbitone, rifabutin, rifampicin); incompatible with erythromycin, hydrocortisone sodium succinate, novobiocin, polymyxin B, tetracycline, vancomycin; safe in pregnancy; very weak association with oral contraceptive failure

Contraindications: avoid if breast feeding (not topical); caution in neonates

THIAMPHENICOL: as for chloramphenicol but stated not to cause irreversible aplasia

MACROLIDES: inhibit protein synthesis by binding 50S ribosomal subunit; bacteriostatic; wide spectrum of activity, including Gram positive cocci, *Legionella*, *Bordetella*, *Corynebacterium*, Gram negative cocci, *Mycoplasma*, *Chlamydia* and Gram positive and Gram negative anaerobes; in Australia, *Moraxella catarrhalis* 3% resistant, *Staphylococcus aureus* 34% resistant overall (methicillin susceptible strains 13% resistant), *Streptococcus pneumoniae* 12% resistant, *Streptococcus pyogenes* 8% resistant

Side Effects: nausea, vomiting, diarrhoea, abdominal pain, cramps, headache, dyspnoea, cough, candidal infections common; rash, fixed drug eruptions, thrombophlebitis (i.v.), QT interval prolongation uncommon; anaphylaxis, acute respiratory distress, Stevens-Johnson syndrome, cholestatic hepatitis, psychiatric disturbances, hearing loss, pseudomembranous colitis, arrhythmias (i.v.) rare; increased risk of ergotism with ergot derivatives; increase concentration of carbamazepine and valproate by CYP3A4 inhibition (avoid combination); combination of some antipsychotics, cyclic antidepressants, fluoxetine or venlafaxine with macrolides can potentiate QT prolongation (avoid)

ERYTHROMYCIN: macrolide; oral (twice daily) except for lactobionate; erythromycin base and erythromycin stearate ½ -1 h before food, estolate and ethylsuccinate does not matter; acts on 50S ribosome to inhibit peptide bonding, acts on transpeptidation and translocation; variable absorption; 41% bronchial penetration 2-3 h after 0.5 mg i.v. dose; serum protein binding 70%; moderate to high postantibiotic effect; bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; spectrum includes *Actinomyces* (good activity), *Bacteroides, Bordetella, Borrelia burgdorferi* (MIC 0.01-1 mg/L), *Capnocytophaga canimorsus* (95% susceptible), *Chlamydia trachomatis* (0.5 mg/L), *Clostridium perfringens* (good activity), *Corynebacterium diphtheriae* (resistance not yet confirmed in Australia), *Erysipelothrix* (100% susceptible at 0.25 mg/L), *Eubacterium* (good activity), *Haemophilus influenzae*, *Legionella* (≤ 0.06-0.5 mg/L), *Listeria monocytogenes* (0.25 mg/L), *Moraxella catarrhalis* (3% resistance in Australia), *Mycobacterium chelonae*, *Neisseria gonorrhoeae* (1 mg/L), *Mycoplasma*, *Rickettsia rickettsii*, *Rickettsia typhi*, *Staphylococcus aureus* (34% resistant in Australia); Enterobacteriaceae, *Pseudomonas* 100% intrinsic resistance; in Australia, *Streptococcus pyogenes* 8% resistant, *Streptococcus pneumoniae* 12% resistant; no effect on opsonisation, decreases chemotaxis, increases neutrophil penetration, reduces release of chemoattractants; minimal inoculum effect; in WHO Model List of Essential Drugs; mode of elimination hepatic

Indications: alternative to penicillin in hypersensitive patients; abortional and puerperal infections; actinomycosis; anthrax; reactive arthritis due to *Campylobacter*, *Chlamydia*; septic arthritis due to *Neisseria*, *Corynebacterium*; bacillary angiomatosis; bacillary peliosis; bacteremia and septicemia (infection from respiratory system in adults); balanitis; bronchiectasis; acute mycoplasmal bronchiolitis and bronchopneumonia; diffuse panbronchiolitis (anti-inflammatory effect); cat scratch disease; cellulitis (mild streptococcal, staphylococcal or clostridial in penicillin hypersensitive); chancroid (drug of choice); chlamydial lymphogranuloma; cholangitis and cholecystitis; cholera; chondritis; bacterial croup; conjunctivitis (chlamydial treatment and prophylaxis; neonatal gonococcal prophylaxis); diphtheria treatment, prophylaxis and carriers; disseminated gonococcal and meningococcal disease; chlamydial dysuria-frequency syndrome; endocarditis due to *Legionella*, *Mycobacterium chelonae*, *Mycobacterium fortuitum*, *Campylobacter* enterocolitis; acute epiglottitis; erysipelas; erysipeloid; erythrasma; erythema chronicum migrans; furuncles; gingivitis and periodontitis in penicillin hypersensitive; gonorrhoea; granuloma inguinale (pregnant or breast-feeding); hepatitis due to *Campylobacter jejuni*, *Coxiella burnetii*, *Actinomyces*; hordeolum; severe impetigo

with cellulitis; ischiorectal abscess; laryngotracheitis; mastitis; myocarditis and pericarditis due to *Actinomyces*, *Campylobacter jejuni*, *Mycoplasma*, *Ureaplasma*; nasopharyngitis; ornithosis; otitis media due to *Corynebacterium bovis;* otitis externa due to *Corynebacterium diphtheriae*, *Actinomyces israelii*, *Staphylococcus aureus*; sexually acquired parametritis; pelvic sepsis and pelvic inflammatory disease; perichondritis; peritonsillar abscess; pertussis treatment and prophylaxis in close contacts; pharyngitis; pneumonia (mild community acquired in child 3 w - 3 mo, mild to moderate community acquired in adult < 60 years and with no coexisting illness and in child 3 mo - 10 y if *Mycoplasma* pneumoniae suspected, severe community acquired in adult, mild to moderate nosocomial in patient on high dose steroids, severe nosocomial, streptococcal, meningococcal, chlamydial; due to *Moraxella catarrhalis, Legionella pneumophila;* diffuse interstitial pneumonia and pneumonitis due to *Corynebacterium equi*); diffuse or interstitial pneumonitis in granulocytopenia; postpartum fever and endometritis; proctitis due to *Campylobacter*, *Chlamydia trachomatis*; prostatitis and seminal vesiculitis; *Haemophilus influenzae* pulmonary infection in cystic fibrosis; acute Q fever; rat bite fever; louse-borne relapsing fever; rape prophylaxis; rheumatic fever treatment and prophylaxis; scarlet fever; local and generalised sepsis due to *Staphylococcus aureus*, *Campylobacter fetus* subsp *fetus*; acute maxillary sinusitis; treatment and prophylaxis of localised skin infections due to *Streptococcus pyogenes*, *Neisseria*, *Staphylococcus aureus*, *Listeria monocytogenes, Arcanobacterium haemolyticum, Corynebacterium bovis*; surgical prophylaxis (post-splenectomy in > 2 years old); granulomatous synovitis due to *Mycobacterium chelonae*; syphilis (penicillin hypersensitive pregnant); tenosynovitis due to *Mycobacterium nonchromogenicum*; tetanus; throat infections due to streptococci, *Corynebacterium*, *Arcanobacterium haemolyticum;* tooth abscess in penicillin hypersensitive; toxic shock syndrome due to *Campylobacter intestinalis;* trachoma; non-gonococcal urethritis; vaginitis due to *Chlamydia trachomatis*, *Mycoplasma hominis*

Side Effects: rare hypersensitivity reactions, frequent gastrointestinal disturbances (nausea, vomiting, diarrhoea after large doses; abdominal pain or nausea in 27% after infusion; pyloric stenosis in < 1 mo old), pseudomembranous colitis, uncommon skin reactions; pain, local reaction and phlebitis at injection site with 1 g doses (i.v. should be administered slowly to minimise local reactions and avoid arrhythmias); reversible jaundice with erythromycin estolate given for > 10-14 d; dizziness; CNS toxicity and rare ototoxicity following i.v. in renal insufficiency (avoid daily dose of > 2 g in severe renal insufficiency); increases risk of infantile hypertrophic pyloric stenosis in early infancy; dose adjustment not required in dialysis (except continuous venovenous or arteriovenous haemodialysis); safe in pregnancy; safe in breastfeeding but monitor infant for diarrhoea; risk of peripheral ischemia with ergotamine; risk of cardiac arrhythmias with astemizole and terfenadine (which have resulted in deaths); may increase plasma levels and effects of amprenavir, buspirone, carbamazepine, cyclosporin, digoxin, theophylline (may cause toxicity), warfarin; ritonavir, amprenavir increase plasma levels; increased risk of QT prolongation with all drugs prolonging QT interval; synercid may increase toxicity; incompatible with ampicillin, carbenicillin, cephalothin, chloramphenicol, cloxacillin, heparin, methicillin, novobiocin, streptomycin, tetracycline; very weak association with oral contraceptive failure

Contraindications: avoid estolate and propionate forms in liver dysfunction

TRIACETYLOLEANDOMYCIN: macrolide; substitute for erythromycin

Side Effects: reversible jaundice if given for > 10-14 d; increase in serum theophylline levels may result in toxicity; risk of peripheral ischemia with ergotamine

SPIRAMYCIN: macrolide

Indications: gonorrhoea, non-specific urethritis

Side Effects: uncommon hypersensitivity and skin reactions, gastrointestinal disturbances; safe in pregnancy

ROXITHROMYCIN: macrolide; good oral bioavailability; usual dose 150 mg orally 12 hourly (1/2 -1 h before food); covers most common respiratory pathogens, including *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*, though some uncertainty about coverage of *Haemophilus influenzae*; and also Gram positive cocci, *Legionella, Corynebacterium,* Gram negative cocci, Gram positive and Gram negative anaerobes but not enteric Gram negative bacilli; more reliable absorption and longer half life than erythromycin but more expensive

Indications: has rapidly earned a place in treatment of respiratory tract infections (bronchitis, mycoplasmal and chlamydial pneumonia, acute streptococcal throat infections, mild to moderate community acquired pneumonia in adult > 60 y or with coexisting illness) in general practice; also bacterial balanitis; cat scratch disease; chlamydial lymphogranuloma; less severe erysipelas in penicillin hypersensitive; gingivitis and periodontitis in penicillin hypersensitive; granuloma inguinale in pregnant or breastfeeding; severe impetigo; sexually acquired parametritis, pelvic sepsis and pelvic inflammatory disease; postpartum fever and endometritis; post-splenectomy prophylaxis; tooth abscess in penicillin hypersensitive; vaginitis

Side Effects: causes less gastrointestinal upset than erythromycin; probably safe in pregnancy; safe in breastfeeding; may increase plasma levels and effects of ergot alkaloids, theophylline and warfarin; possibility of interaction with astemisole and terfenadine; dose adjustment not required in renal failure or in dialysis

CLARITHROMYCIN: only macrolide with microbiologically active metabolite; usual dose 250 mg orally 12 hourly (relationship of dose to food doesn't matter); activity similar to erythromycin + activity against *Mycobacterium avium*; concentration in

alveolar macrophages ≈ 100X greater than in plasma or serum; considerably more expensive than erythromycin and roxithromycin

Indications: at present, use largely confined to treatment of non-tuberculous mycobacterial infections, especially *Mycobacterium avium* lung disease and disseminated infections in AIDS patients; also respiratory tract infection with *Legionella, Streptococcus pneumoniae, Haemophilus influenzae* if intolerant of erythromycin; simple gastritis, duodenal ulcer and peptic ulcer due to *Helicobacter pylori*

Side Effects: gastrointestinal intolerance; infusion site pain in 92%, phlebitis and inflammation, hypersensitivity syndrome, fixed drug reaction, pustulosis, vasculitis; increased risk of fatal bone marrow toxicity in combination with colchicine; potential to prolong QT interval; may increase plasma levels and effects of some antihistamines (astemizole, terfenadine; risk of cardiac arrhythmias, which have resulted in deaths), carbamazepine, cisapride (increased risk of QT prolongation), cyclosporin, digoxin, fluconazole, itraconazole, rifabutin (may cause uveitis), theophylline, warfarin; plasma levels reduced by rifabutin and rifampicin; lopinavir, ritonavir increase plasma levels; reduces bioavailability of zidovudine (space 2 h apart); delavirdine, ritonavir may increase toxicity; adjustment required in renal failure and in dialysis

Contraindications: safety in pregnancy not established; caution if breastfeeding (safety not established), monitor infant for diarrhoea

AZITHROMYCIN: oral macrolide (timing to food does not matter); good in vitro activity against a wider range of organisms than erythromycin, including greater activity against *Haemophilus influenzae*, but less active against Gram positives (though active against nontuberculous mycobacteria, including *Mycobacterium avium* complex); first agent shown to be effective in a single dose for uncomplicated *Chlamydia trachomatis* infections of genital tract; also covers *Neisseria gonorrhoeae*; good oral bioavailability and rapid and sustained uptake by tissues; concentration in alveolar macrophages ≈ 100X greater than in serum or plasma; once daily dosing and long half life; considerably more expensive than erythromycin but better gastrointestinal tolerability

Indications: cat scratch disease; cerebral toxoplasmosis in AIDS; chancroid; chlamydial conjunctivitis; chlamydial lymphogranuloma; granuloma inguinale; *Mycobacterium avium-intracellulare* prophylaxis and pulmonary tuberculosis; respiratory tract infection due to *Chlamydia, Haemophilus influenzae, Moraxella, Mycoplasma, Streptococcus pneumoniae* when erythromycin not tolerated; trachoma; uncomplicated urethritis and cervicitis due to *Chlamydia trachomatis*; vaginitis

Side Effects: gastrointestinal intolerance, reversible ototoxicity, hypersensitivity syndrome, fixed drug reaction, photosensitivity, pustulosis; bioavailability reduced by antacids and didanosine (space doses by 2-3 h); causes high plasma levels of astemizole and terfenadine, with risk of cardiac arrhythmias; ritonavir, saquinavir increase plasma levels; antacids reduce bioavailability (space 2-3 h apart); dose adjustment required in renal failure and in dialysis; less likely enhanced warfarin effect (safest of macrolides); probably safe in pregnancy

Contraindications: avoid in breastfeeding (insufficient data); infants < 6 kg

ERYTHROMYCIN + SULPHISOXAZOLE: moderately expensive; oral dosing schedule 4 times daily; spectrum includes *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*

Indications: acute otitis media

Side Effects: high risk of serious adverse reactions and gastrointestinal adverse effects, moderate risk of skin rash

LINCOSAMIDES: inhibit protein synthesis by binding 50S ribosomal subunit; active against Gram positive aerobes and most anaerobes

Indications: should be used as second choice in those who cannot tolerate conventional therapy

Side Effects: antimicrobial-associated diarrhoea, colitis, nausea, vomiting, abdominal cramps, abdominal pain, metallic taste (i.v.), itch, rash, contact dermatitis (topical) common; anaphylaxis, blood dyscrasias, polyarthritis, jaundice, hepatotoxicity (high doses), thrombophlebitis (i.v.), pain, induration, sterile abscess (i.m.), hypotension, cardiac arrest (rapid i.v.) rare

CLINDAMYCIN: lincosamide; oral (relationship of dose to food doesn't matter) and i.v. (administer slowly (may cause serious arrhythmias); considerably more expensive than lincomycin); also cream, lotion, gel; acts on 50S ribosome to inhibit peptide bonding and protein synthesis; bacteriostatic; time-dependent killing; well absorbed; distributes well into multiple tissues; very good intracellular and tissue penetration (except CNS), including abscesses; 61% bronchial penetration after 0.3 g oral dose; very large postantibiotic effect; increases opsonisation, increases phagocytosis, reduces bacterial adherence, reduces capsule enzyme/toxin, increases neutrophil penetration, increases intracellular killing; kills bacteria phagocytosed by granulocytes; no inoculum effect; mode of elimination hepatic; active against Gram positive aerobes, including methicillin sensitive *Staphylococcus aureus,* and most anaerobes; spectrum includes *Actinomyces* (85-100% susceptible), anaerobic cocci (97% susceptible), *Arachnia* (85-100% susceptible), *Bacteroides* (good activity; 97-99% susceptible, including 81% of *Bacteroides fragilis* group but only 59% of *Bacteroides thetaiotaomicron*, *Bacteroides bivius* MIC < 0.25 mg/L), *Capnocytophaga canimorsus* (98% susceptible), *Clostridium* (good activity except *Clostridium difficile*; 88% susceptible at < 1 mg/L), *Erysipelothrix* (100% susceptible at 0.25 mg/L), *Flavobacterium odoratum* (0.13-1 mg/L), *Fusobacterium* (good activity except *F.varium*; 92% susceptible), *Peptococcus* (< 1 mg/L), *Peptostreptococcus* (< 1 mg/L), *Prevotella melaninogenica* (≤ 0.25 mg/L), *Propionibacterium acnes, Staphylococcus aureus* (95% susceptible), *Streptococcus canis* (0.12 mg/L); Enterobacteriaceae 100% intrinsic resistance, *Enterococcus* 100% intrinsic resistance, *Pseudomonas* 100% intrinsic resistance;

in WHO Model List of Essential Drugs as complementary drug when drugs in the main list are known to be ineffective or inappropriate for a given individual

Indications: should be used as second line agent in patients who cannot tolerate conventional therapy, especially for staphylococcal (including community-associated methicillin resitant *Staphylococcus aureus*) and streptococcal infections (including scarlet fever), lung, dental and peritonsillar abscesses; also abortional and puerperal infection; abdominal sepsis; moderate acne vulgaris and rosacea (topical); septic arthritis due to *Staphylococcus aureus* in penicillin hypersensitive; bacteraemia and septicemia (focus probably biliary or gastrointestinal tract or open skin infection/cellulitis; due to *Leuconostoc*, due to *Streptococcus pyogenes* in penicillin hypersensitive); brain and epidural abscess; burn infection due to *Flavobacterium meningosepticum*; cellulitis due to *Staphylococcus aureus* or *Streptococcus pyogenes* in severely penicillin hypersensitive; cervical fascial space infections in normal patients; anaerobic empyema; endocarditis treatment and prophylaxis; postpartum fever and endometritis; intraabdominal abscess; iridocyclitis due to *Bacillus;* myocarditis and pericarditis due to *Actinomyces*; necrotising fasciitis due to *Streptococcus pyogenes*; necrotising ulcerative gingivostomatitis in penicillin hypersensitive; osteomyelitis and osteochondritis (due to *Staphylococcus aureus* in penicillin hypersensitive, due to anaerobes); panophthalmitis due to *Bacillus cereus*; parametritis; anaerobic parotitis and submandibular sialadenitis; pelvic inflammatory disease and pelvic sepsis due to trauma; perianal and perirectal abscess and cellulitis in patients with malignant disease; anaerobic pleuropulmonary infections; pneumonia (mild to moderate nosocomial associated with aspiration or thoracoabdominal surgery); salpingitis; scarlet fever; local and generalised sepsis due to anaerobes, *Bacillus cereus*; severe infections in penicillin allergic patients; chronic sinusitis; localised skin lesions; acute skin ulcers due to *Flavobacterium meningosepticum*; soft tissue infection in anogenital region; symbiotic gangrene; systemic infection in granulocytopenia (severe oral mucositis or necrotising gingivitis, perianal tenderness); toxic epidermal neurolysis; staphylococcal toxic shock syndrome; tubo-ovarian abscess; vaginosis in pregnancy (topical)

Side Effects: uncommon hypersensitivity reactions, gastrointestinal disturbances (diarrhoea in 0.3-21%, pseudomembranous colitis in 2-10%), skin reactions (rashes, Stevens-Johnson syndrome, vasculitis) in 8%; tinnitus; hepatotoxicity in 1%; may increase and prolong neuromuscular blockade produced by neuromuscular blockers; may increase saquinavir levels; dosage modification not required in renal dysfunction or in dialysis; reduce dosage to 1/3 – ½ normal in liver dysfunction; safe in pregnancy; very weak association with oral contraceptive failure

Contraindications: avoid in patients over 60 and those with a history of cardiovascular disease or treatment with anticholinergics; safe in breastfeeding but monitor infant for diarrhoea

LINCOMYCIN (LINCOCIN): lincosamide; now only available as parenteral formulation (considerably cheaper than clindamycin); bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; mainly active against Gram positive bacteria; spectrum includes *Bacteroides*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*; increases opsonisation, chemotaxis, phagocytosis, reduces capsule enzyme/toxin, increases neutrophil penetration and intracellular killing

Indications: abdominal sepsis; empyema; endocarditis due to *Fusobacterium*, *Prevotella;* putrid lung abscess; osteomyelitis; acute lobar pneumonia; chronic Q fever; septicemia; severe infections in penicillin allergic patients; chronic sinusitis, soft tissue infection in anogenital region; colon and uterus surgical prophylaxis

Side Effects: uncommon hypersensitivity reactions, serum sickness-like illness, gastrointestinal disturbances (diarrhoea, pseudomembranous colitis), skin reactions (photosensitivity), ? cardiopulmonary arrest after rapid i.v. infusion; modify dosage interval in renal dysfunction; dose adjustment not required in dialysis (except in continuous venovenous or arteriovenous haemodialysis); safe in pregnancy; caution in breastfeeding (monitor infant for diarrhoea); serum levels markedly decreased by kaolin-pectin suspension and cyclamate diet drink (give 2 h apart); incompatible with ampicillin, benzylpenicillin, carbenicillin, cephalothin, colistimethate, kanamycin, novobiocin

TELITHROMYCIN: ketolide; spectrum includes *Actinomyces* (MIC ≤ 0.015 mg/L), *Bordetella pertussis* (0.03 mg/L), *Bordetella parapertussis* (0.25 mg/L), *Chlamydia trachomatis* (0.12 mg/L), *Clostridium perfringens* (0.06-0.25 mg/L), *Helicobacter pylori* (0.5 mg/L), *Lactobacillus* (0.015-0.03 mg/L), *Legionella pneumophila* (0.004-0.12 mg/L), *Leuconostoc* (0.015-0.06 mg/L), *Listeria monocytogenes* (0.06-0.25 mg/L), *Moraxella catarrhalis* (0.008-0.25 mg/L), *Mycoplasma pneumoniae* (0.00025-0.015 mg/L), *Neisseria gonorrhoeae* (0.03-0.5 mg/L), *Neisseria meningitidis* (0.03-0.5), *Porphyromonas* (< 0.016-0.25 mg/L), methicillin sensitive *Staphylococcus aureus* (0.06-0.25 mg/L), methicillin sensitive coagulase negative *Staphylococcus* (0.25-0.5 mg/L), *Streptococcus agalactiae* (0.015-0.06 mg/L), *Streptococcus canis* (0.06 mg/L), *Streptococcus pneumoniae* (≤ 0.004-0.5 mg/L; including strains resistant to other antibiotics), *Streptococcus pyogenes* (0.008-1 mg/L), group C streptococci (0.06 mg/L), group F streptococci (0.03 mg/L), viridans group streptococci (≤ 0.004-0.25 mg/L), *Ureaplasma urealyticum* (0.03-0.06 mg/L)

Indications: community acquired pneumonia, acute exacerbation of chronic bronchitis, acute sinusitis

Side Effects: diarrhoea, nausea, exacerbation of myasthenia gravis

TETRACYCLINE: oral (take ½ -1 h before food) and parenteral; acts on 30S ribosome to inhibit binding of amino-acyl-tRNA, acts on codon recognition and translocation; usually bacteriostatic; no significant change in absorption in elderly; low to

moderate postantibiotic effect; bacteriostatic and bactericidal in high concentrations; lethal for proliferating bacteria and bacteria in latent phase; penetrates well into mammalian cells; active against Gram positive and Gram negative bacteria; spectrum includes *Actinomyces*, *Bacteroides*, *Borrelia recurrentis*, *Brucella* (MIC ≤ 0.13-0.25 mg/L), *Cardiobacterium hominis, Chlamydia,* coliforms, *Fusobacterium* (good activity except *F.varium*), *Haemophilus influenzae* (5% resistance in Australia), *Helicobacter pylori*, *Listeria monocytogenes* (0.5 mg/L), *Moraxella catarrhalis* (0.8% resistance in Australia), some nontuberculous *Mycobacteria, Mycoplasma*, *Brevundimonas vesicularis* (0.13-1 mg/L), *Rickettsia, Salmonella*, *Shigella*, some spirochaetes, *Yersinia*; *Serratia marcescens* 100% resistant, *Streptococcus agalactiae* 79% acquired resistance, *Proteus mirabilis* 98% intrinsic resistance (possibly all resistant in clinical practice); in Australia, *Streptococcus pneumoniae* 13% resistant, *Neisseria gonorrhoeae* 5% high level resistance, *Staphylococcus aureus* 5% methicillin susceptible strains resistant (23% overall); 36% protein binding; reduces bacterial adherence and intracellular killing, reduces release of chemoattractants, inhibits chemotactic activity of granulocytes, diminishes phagocytosis; no inoculum effect; mode of elimination renal, hepatic

Indications: reduced value due to emergence of resistant strains and development of other antimicrobial agents; moderate to severe acne vulgaris; actinomycosis; anthrax; reactive arthritis due to *Shigella, Salmonella, Yersinia, Chlamydia;* septic arthritis due to *Mycoplasma hominis*, *Ureaplasma urealyticum*; bacillary angiomatosis; bacillary peliosis; bartonellosis; bacterial blepharitis; boils; bronchiectasis and chronic bronchitis in patients > 8 y of age; brucellosis; carbuncles; cellulitis due to *Vibrio*; chancroid; cholera; purulent conjunctivitis (treatment of more severe; prophylaxis of chlamydial and neonatal gonococcal); bacterial dysentery; chlamydial dysuria-frequency syndrome; ehrlichiosis; endocarditis due to *Fusobacterium*, *Prevotella, Coxiella burnetii;* acute epididymitis and epididymoorchitis; erythema chronicum migrans; erythema serpens; furuncles; gas gangrene in penicillin allergic patient; simple gastritis, duodenal ulcer and peptic ulcer; gonorrhoea (including acute throat infections); granuloma inguinale; hepatic abscess due to *Actinomyces*; hepatitis due to *Coxiella burnetii*, *Rickettsia*, *Actinomyces*, *Borrelia recurrentis*, *Yersinia pseudotuberculosis;* severe leptospirosis; Lyme disease; myocarditis and pericarditis due to *Actinomyces*, *Actinobacillus actinomycetemcomitans*, *Rickettsia rickettsii, Mycoplasma, Ureaplasma; Neisseria meningitidis* carriers; ornithosis; pyogenic osteomyelitis and osteochondritis due to *Vibrio vulnificus;* otitis externa due to *Actinomyces israelii*; treatment of sexual partners of patients with parametritis, pelvic sepsis, pelvic inflammatory disease; periodontal disease; peritonitis of suspected bowel origin; plague; community acquired pneumonia and pneumonia due to *Francisella tularensis*, *Vibrio vulnificus;* pneumonitis due to *Francisella tularensis*; chlamydial proctitis; prostatitis; pseudotuberculosis; Q fever; rape prophylaxis; rat bite fever; relapsing fever treatment and prophylaxis; acute respiratory illness due to *Mycoplasma pneumoniae*, *Coxiella burnetii*; rickettsioses, local and generalised sepsis due to *Vibrio*, *Clostridium botulinum;* acute maxillary sinusitis; localised skin lesions due to *Staphylococcus aureus*, *Rickettsia*; acute skin ulcers due to *Francisella tularensis*; stye; surgical prophylaxis in ruptured, perforated or gangrenous viscus (lavage); sycosis barbae; syphilis in penicillin allergic patient; systemic infection prophylaxis in agammaglobulinemia; acute throat infections due to *Mycoplasma pneumoniae*, *Chlamydia*; tracheitis; trachoma treatment and prophylaxis; bacterial vaginitis; non-gonococcal venereal infections; water-related infections

Side Effects: allergic reactions (rare); disorders of gastrointestinal tract (nausea, vomiting, epigastric burning, diarrhoea common; esophageal ulcers, enterocolitits, pseudomembranous colitis rare) and CNS (rare benign intracranial hypertension in newborn); rash, stomatitis, overgrowth of resistant organisms (eg., *Candida albicans*), photosensitivity uncommon; permanent discolouration of children's teeth and nails, bone deformity, reduced bone growth if given after 18th week of pregnancy or to children < 8 y; raises blood urea; hepatotoxicity (hepatitis, fatty liver degeneration) in pregnancy with large doses given parenterally; pain and local reaction at injection site; Fanconi-like syndrome with outdated products; nephrotoxicity; exacerbation of systemic lupus erythematosus (rare); worsening uremia and acidosis in renal insufficiency (avoid; use doxycycline when a tetracycline is indicated); avoid in dialysis; maximum permissible blood level 20 mg/L; bioavailability decreased by most liquid antacids, tri-potassium and di-citrato bismuthate, calcium preparations, aluminium, sodium, magnesium, didanosine, iron hematinics (absorption of iron also markedly decreased), sucralfate, zinc sulphate, kaolin + pectin (space doses by 2-3 h); activity of warfarin may be increased; incompatible with ampicillin, carbenicillin, cephalothin, chloramphenicol, cloxacillin, erythromycin, heparin, methicillin, novobiocin, penicillin, polymyxin B; weak association with oral contraceptive failure

Contraindications: renal failure; pregnancy after 18th week; avoid if breastfeeding (7-10 d course probably safe); children < 8 y

CHLORTETRACYCLINE: oral preparation no longer available

DEMECLOCYCLINE: tetracycline; give on empty stomach

Side Effects: greater risk of photosensitivity than with other tetracyclines

DOXYCYCLINE: binds to 30S ribosome, preventing tRNA docking and inhibiting protein synthesis; bacteriostatic to bactericidal; time-dependent killing; oral tetracycline (take after food with full glass of water and remain upright for at least 30 min; once daily dosing); good absorption, but reduced by coadministration with cations; widely distributed; nonrenal excretion; best pharmacology of tetracyclines (with minocycline) makes it preferred tetracycline in most situations; 35% bronchial penetration 2-3 h after 0.1 g oral dose; no significant change in V_d in elderly; 70% protein binding; spectrum includes *Acinetobacter lwoffi* (MIC 0.06-1 mg/L), *Bordetella bronchiseptica* (0.06-0.25 mg/L), *Chlamydia*, *Mycoplasma hominis*,

Brevundimonas vesicularis (≤ 0.03-0.25 mg/L); in WHO Model List of Essential Drugs; mode of elimination renal and hepatic, non-renal in patients with renal failure

Indications: moderate to severe acne; reactive arthritis due to *Chlamydia*; septic arthritis due to *Brucella*, *Mycoplasma hominis*, *Ureaplasma urealyticum;* bacillary angiomatosis; bacillary peliosis; bronchiectasis in patients > 8 y; chronic bronchitis in patients > 8 y; brucellosis; cat and dog and human bite and clenched fist injury infections in penicillin hypersensitive nonpregnant adults; cat scratch disease; mycoplasmal cellulitis; chlamydial lymphogranuloma; acute cholecystitis; cholera; chlamydial conjunctivitis in nonpregnant adults; bacterial dysentery; chlamydial dysuria-frequency syndrome; ehrlichiosis; encephalitis due to *Chlamydia*, *Mycoplasma*, *Rickettsia*; endocarditis due to *Brucella*; endometritis; sexually acquired acute epididymitis and epididymoorchitis; gonorrhoea; granuloma inguinale; severe leptospirosis; Lyme disease (arthritis, Bell's palsy, mild cardiac disease); melioidosis; meningitis due to *Brucella*; meningoencephalitis due to *Coxiella burnetii*, *Mycoplasma*; chlamydial; orchitis; ornithosis; acute bacterial otitis media; osteomyelitis and osteochondritis due to *Brucella;* parametritis; pelvic inflammatory disease; sexually acquired pelvic sepsis; perihepatitis; peritonitis suspected associated with pelvic inflammatory disease; pneumonia (mild to moderate community acquired in adult, mycoplasmal, chlamydial, *Legionella pneumophila*); chlamydial proctitis; prostatitis and seminal vesiculitis; acute Q fever; rape prophylaxis; rickettsioses treatment and prophylaxis; salpingitis; syphilis in penicillin hypersensitive nonpregnant; tick-borne relapsing fever; trachoma in nonpregnant adult; traveller's diarrhoea prophylaxis in high risk host; non-gonococcal or post-gonococcal urethritis, cervicitis due to *Chlamydia, Trichomonas*; vaginitis due to *Chlamydia trachomatis*, *Mycoplasma hominis*

Side Effects: nausea, vomiting, diarrhoea, allergic reactions (rare), esophagitis (wash down well and remain upright at least 30 minutes after administration), photosensitivity, vaginal thrush; does not raise blood urea; does not require dosage modification in renal dysfunction or in dialysis; bioavailability decreased by antacids, iron and calcium preparations but not by zinc sulphate; plasma levels may be reduced by carbamazepine, phenobarbitone and phenytoin; weak association with oral contraceptive failure

Contraindications: > 18 w pregnant; use in breastfeeding only if ≤ 10 d course and alternative drugs not appropriate; children < 8 y (though less permanent discolouration of children's teeth and nails than with tetracycline)

METHACYCLINE: oral tetracycline (take ½ - 1 h before food); bioavailability reduced by antacids, didanosine, iron and calcium preparations (space doses by 2-3 h)

MINOCYCLINE: oral tetracycline (take with or after food); best pharmacology of tetracyclines (with doxycycline); mode of elimination renal, hepatic; active against some strains of tetracycline-resistant bacteria, including strains of staphylococci; spectrum includes *Acinetobacter lwoffi* (MIC 0.06-1 mg/L), *Borrelia burgdorferi* (0.09-0.25 mg/L), *Bordetella bronchiseptica* (0.13-1 mg/L), *Comamonas terrigena* (0.06-4 mg/L), *Moraxella* (0.25-1 mg/L), *Nocardia*, *Brevundimonas diminuta* (0.13-2 mg/L), *Brevundimonas vesicularis* (≤ 0.03-0.5 mg/L)

Indications: severe acne not responding to other tetracyclines; bacillary angiomatosis; bacillary peliosis; fish spine injuries and other water-related infections due to *Vibrio;* meningitis due to *Acinetobacter*, *Nocardia asteroides*; nocardiosis; pneumonitis due to *Mycoplasma pneumoniae*, *Nocardia asteroides*; less severe acute prostatitis and seminal vesiculitis; nongonococcal urethritis

Side Effects: as for tetracycline but higher incidence of vestibular adverse effects; also benign intracranial hypertension (risk increased with etretinate, isotretinoin), skin pigmentation; dose adjustment not necessary in renal failure or in dialysis; weak association with oral contraceptive failure; bioavailability reduced by antacids, didanosine, iron and calcium preparations (space doses by 2-3 h)

Contraindications: pregnancy after first 18 w

TIGECYCLINE: glycylglycine derivative of minocycline; binds to 30S ribosome, preventing tRNA docking and inhibiting protein synthesis; bacteriostatic; time-dependent killin; AUC:MIC may be best predictive e parameter; wide tissue distribution; low serum concentration; nonrenal elimination; active against *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella penumoniae*, *Streptococcus pyogenes*, *Acinetobacter baumannii*, most Enterobacteriaceae, *Bacteroides*, *Clostridium perfringens*; not active against *Pseudomonas aeruginosa*, *Proteus*

Side Effects: nausea, vomiting, diarrhoea

OXYTETRACYCLINE: oral preparation no longer available

Indications: bronchitis prophylaxis; endocarditis due to *Brucella*; hepatitis due to *Leptospira*; leptospirosis

Side Effects: less permanent discolouration of children's teeth and nails than with tetracycline

Contraindications: avoid in renal failure (azotemia, nephrotoxicity) and pregnancy

NITROFURANTOIN: nitrofuran; exact mechanism of action uncertain; may have several bacterial enzyme targets and directly damage DNA; oral (take with or after food (absorption enhanced)); activity reduced in alkaline urine; in WHO Model List of Essential Drugs as complementary drug when drugs in main use or known to be ineffective or inappropriate for a given individual and for which adverse effects diminish benefit/risk ratio; mode of elimination renal; *Serratia marcescens* 100% resistant, *Proteus mirabilis* 95% intrinsic resistance (possibly all resistant in clinical practice)

Indications: used occasionally for urinary tract infection (acute cystitis) and prevention of recurrent urinary tract infection

Side Effects: hypersensitivity reactions (allergic skin reactions common), gastrointestinal disturbances (nausea, vomiting common; abdominal pain, diarrhoea uncommon), ascending peripheral polyneuropathy with high blood levels or in presence of renal failure, hemolytic anemia (mainly in those with glucose-6-phosphate dehydrogenase deficit); severe acute or chronic pulmonary reactions (pneumonitis, fibrosis), nephrotoxicity, chronic active hepatitis, acute hepatocellular or cholestatic reaction rare; *Clostridium* difficile-assocaited diarrhoea; avoid in moderate to severe renal dysfunction (glomerular filtration rate < 50 mL/min) and in dialysis; safe in pregnancy

Contraindications: avoid if breastfeeding premature infant, < 1 mo old or with G6PD deficiency

Hexamine (Methenamine) Mandelate and Hippurate: concentrates in urine, where it is converted to formaldehyde (active agent); requires acidification and long dwell time; oral (not affected by food)

Indications: used occasionally for urinary tract infection and prevention of recurrent acute cystitis

Side Effects: gastrointestinal and skin reactions; dose adjustment not required in dialysis (except in continuous venovenous and arteriovenous hemodialysis); activity decreased by urinary alkalinisers (eg, acetazolamide, sodium bicarbonate); safe in pregnancy

Contraindications: avoid in severe renal failure (glomerular filtration rate < 10 mL/min; ineffective; seizures) and in dialysis; avoid in brrestfeeding (insufficient data)

Nitroimidazoles: spectrum of activity encompasses Gram negative and Gram positive anaerobes

Side Effects: nausea, diarrhoea, metallic taste, thrombophlebitis (i.v.) common; rash, itch, dizziness, vomiting, glossitis, stomatitis, paraesthesia uncommon; colitis, pancreatitis, hepatitis, anaphylaxis, optic neuritis, peripheral neuropathy, seizures rare

Metronidazole: nitroimidazole; exact mechanism of action uncertain but disrupts DNA; bactericidal; oral (twice daily; take with or after food; benzylmetronidazole, ½ -1 h before food), suppositories and i.v.; good absorption; no significant change in absorption, reduced clearance in elderly; no effect on chemotaxis or intracellular killing; in WHO List of Model Drugs; mode of elimination hepatic and renal; spectrum includes anaerobic cocci (98-99% susceptible), anaerobic Gram negative bacilli (*Bacteroides* good activity; *Bacteroides fragilis* < 5% resistance; *Fusobacterium* good activity, 100% susceptible at < 1 mg/L), anaerobic Gram positive bacilli (*Clostridium* good activity, 99% susceptible; *Clostridium difficile* 100% susceptible at < 1 mg/L)

Indications: anaerobic infections; reactive arthritis due to *Clostridium difficile*; bacteremia and septicemia (infection from female genital tract, focus probably biliary or gastrointestinal tract, focus probably decubitus or ischemic ulcer or diabetic foot ulcer); brain abscess from frontal sinus or due to anaerobes); cat and dog and human bite and clenched fist injury infections in penicillin hypersensitive; anaerobic cellulitis; cervical fascial space infections in normal patient; clostridial myositis/myonecrosis (gas gangrene); cranial parameningeal deep fascial space infections (otogenic, rhinogenic, odontogenic in normal patient); *Clostridium difficile* diarrhoea and pseudomembranous colitis (drug of choice); endocarditis due to *Fusobacterium*, *Prevotella*; endometritis; *Bacteroides* enterocolitis; severe gingivitis and periodontitis; hepatic abscess; intraabdominal infections, ischiorectal abscess; postneonatal pyogenic meningitis due to *Bacteroides*; necrotising enterocolitis due to *Clostridium perfringens;* necrotising fasciitis; gastritis/ulcers due to *Helicobacter pylori*; necrotising ulcerative gingivostomatitis; anaerobic otitis externa; parametritis; pelvic inflammatory disease and pelvic sepsis; perinatal generalised disease due to anaerobes other than *Peptostreptococcus* and *Clostridium*; periodontitis; acute peritonitis associated with appendix etc; moderate to severe anaerobic pleuropulmonary infections; mild to moderate nosocomial pneumonia associated with aspiration or thoraco-abdominal surgery; pulmonary abscess; rape prophylaxis; salpingitis; local and generalised sepsis due to *Clostridium botulinum* or unknown organisms; splenic abscess due to *Clostridium difficile*; surgical prophylaxis (normal labour; colorectal; appendicectomy; hysterectomy; termination of pregnancy; lower limb amputation; ruptured, perforated or gangrenous viscus; muscular, skeletal and soft tissue trauma); symbiotic gangrene; systemic infections in granulocytopenia (severe oral mucositis or necrotising gingivitis, perianal tenderness); severe tooth abscess; tropical ulcer; ulcers in diabetics; treatment failure in nongonococcal urethritis; vaginitis; vaginosis; Vincent's angina

Side Effects: peripheral neuropathy, acute pancreatitis; nausea, drowsiness, headache, rashes, dizziness, vestibular symptoms, ataxia, transient epileptiform seizures with high doses; moderate to significant adjustment of dosage needed in renal failure (vestibular toxicity may occur); dose adjustment required in dialysis; safety in pregnancy not established; marked potentiation of warfarin; may increase plasma levels and effects of cyclosporin, phenytoin, lithium; 'antabuse' syndrome may occur with alcohol; decreased plasma levels with phenobarbitone, cholestyramine, aluminium hydroxide, antacid; weak association with oral contraceptive failure; safety of systemic in pregnancy not established

Contraindications: patients with history of blood disease, patients with acute central nervous system disease; avoid high single dose systemic therapy in breastfeeding

Tinidazole: oral only (take with or after food); longer half life than metronidazole and can be administered less frequently or as a single dose; spectrum includes anaerobic Gram negative bacilli, anaerobic Gram positive bacilli and cocci

Indications: sexually acquired pelvic sepsis in outpatient; surgical prophylaxis (hysterectomy, termination of pregnancy); vaginitis; vaginosis
Side Effects: lassitude, dizziness, bitter taste, nausea, rarely vomiting, diarrhoea, constipation, thirst, sweating, itching; safety in pregnancy not established; disulfiram-like reaction may occur with alcohol; dosage modification not required in renal failure; dose required after intermittent haemodialysis; safety in pregnancy not established
Contraindications: avoid if breastfeeding
NIMORAZOLE
Indications: vaginosis
Contraindications: pregnancy
NOVOBIOCIN: bacteriostatic and bactericidal in high concentrations; acts only on proliferating bacteria; weakly penetrates into mammalian cells and is not lethal for intracellular bacteria; active against Gram positive bacteria; 99% protein binding
Indications: none
Side Effects: hypersensitivity reactions, gastrointestinal disturbances, skin reactions, pain at injection site, blood dyscrasias, hemolytic anemia (mainly in those with glucose-6-phosphate dehydrogenase deficit), hyperbilirubinemia in newborn, yellow discolouration of skin and sclera; maximum permissible blood level 15 mg/L
Contraindications: pregnancy
SODIUM FUSIDATE: oral (take with or after food); bacteriostatic and possibly bactericidal in high concentrations; very active against *Staphylococcus aureus* but resistance develops rapidly; in Australia, methicillin resistant *Staphylococcus aureus* 4% resistant; protein binding 97%
Indications: infections with methicillin resistant *Staphylococcus aureus* (should never be used alone); staphylococcal brain and epidural abscess; *Staphylococcus aureus* pulmonary infection in cystic fibrosis
Side Effects: gastrointestinal disturbances (epigastric discomfort, nausea), thrombophlebitis common; headache uncommon; granulocytopenia, thrombocytopenia, elevated transaminases, jaundice (i.v.), skin reactions (rash) rare; rhabdomyolysis and elevated creatine kinase when combined with statins; dose adjustment not required in renal failure or in dialysis
Contraindications: pregnancy; caution in breastfeeding (insufficient data)
MUPIROCIN: reversibly inhibits isoleucyl tRNA synthetase; active against broad range of Gram positive bacteria, including methicillin resistant *Staphylococcus aureus* (but high level resistance readily selected by prolonged or widespread use); moderately active against *Haemophilus influenzae* and *Neisseria gonorrhoeae*; deleted from WHO Model List of Essential Drugs because expensive and other drugs listed considered adequate
Indications: elimination of nasal carriage of *Staphylococcus aureus* (calcium dihydrate salt in soft paraffin base); impetigo (ointment of free base in polyethylene glycol); probably safe in pegnancy; safe in breastfeeding
Side Effects: local adverse reactions in 2%
FURAZOLIDONE: nitrofuran
Indications: cholera, treatment of enteritis due to *Blastocystis hominis*
Side Effects: tinnitus, hearing loss, vestibular symptoms
OXAZOLIDINONES: new class of agents; inhibit formation of initiation complex; active against Gram positive bacteria (including methicillin resistant *Staphylococcus aureus,* vancomycin resistant *Enterococcus*, resistant *Streptococcus pneumoniae*) and some anaerobic Gram negative bacteria (including *Bacteroides fragilis*)
LINEZOLID: first member of oxazolidinone class; injections, tablets, oral suspension (timing to food does not matter); inhibits protein synthesis by specifically binding to 50S ribosomal subunit, preventing union of 50S and 30S ribosomes; bacteriostatic; time-dependent killing; AUC:MIC and time > MIC predictive parameters; 100% bioavailability after oral dosing; wide tissue and CNS distribution; nonrenal clearance; effective against Gram positive organisms, including methicillin resistant *Staphylococcus aureus*, coagulase negative staphylococci, vancomycin resistant enterococci and penicillin resistant *Streptococcus pneumoniae*; expensive
Indications: reserved for multi-drug-resistant infections (should be commenced in hospital); infections with vancomycin resistant *Enterococcus* (including cases with concurrent bacteremia; 2% develop resistance during therapy); pneumonia caused by *Staphylococcus aureus* or *Streptococcus pneumoniae* (including cases with concurrent bacteraemia); skin and skin structure infections caused by *Staphylococcus aureus, Streptococcus pyogenes* or *Streptococcus agalactiae*
Side Effects: diarrhoea in 8%, headache in 7%, nausea in 6%, vomiting in 4%, tongue discolouration in 3%, thrombocytopenia in 3%, dermatological reactions in 3%, reduced hemoglobin/haematocrit in 0.8%, leucopenia in 0.8%, allergy in 0.3%; abdominal pain, taste disturbance, raised liver enzymes, candidiasis, peripheral neuropathy,optic neuritis common; thrombocytopenia, hypertension, eosinophilia, neutropenia, rash, pruritis, urticaria, thrombophlebitis, dizziness, hypaesthesia, insomnia, paraesthesia, blurred vision, pancreatitis uncommon; myelosuppression, pancytopenia, pseudomembranous colitis rare; monitor platelets if > 2 w of therapy; pure red blood cell aplasia reported; monoamine oxidase inhibitory activity can increase blood pressure if used with pseudoephedrine, phenylpropanolamine, dopamine, adrenaline, tyramine-containing foods and serotonergic drugs; serotonin syndrome on coadministration with serotonergic drugs; safety in pregnancy not established
Contraindications: avoid in breastfeeding

EPEREZOLID: oxazolidinone similar to linezolid

CAPREOMYCIN: antitubercular

Indications: *Mycobacterium* infections (dosage 1 g daily or twice weekly; used infrequently)

Side Effects: ototoxicity, nephrotoxicity, pain on injection, symptomless eosinophilia, drug fever, skin rash, myelosuppression; single case report of hearing loss; possible cumulative nephrotoxicity and ototoxicity with aminoglycosides, high dose aspirin, frusemide, methoxyflurane; may increase neuromuscular blockade with neuromuscular blocking drugs

Contraindications: pregnancy, avoid in breastfeeding (insufficient data)

CYCLOSERINE: bacteriostatic; acts only on proliferating bacteria; penetrates well into mammalian cells; active against *Mycobacterium*; oral (not affected by food)

Indications: *Mycobacterium* infections (dosage 750 mg daily; used infrequently)

Side Effects: CNS reactions (headache, somnolence, mental disturbances, convulsions; seizures controlled by 100 mg pyridoxine daily; CNS toxicity increased by ethionamide, alcohol (increased risk of epileptic episodes), isoniazid); further dose required after hemodialysis; avoid use if possible in renal insufficiency (when indicated, adjust dose appropriately and monitor serum levels); maximum permissible blood level 25 mg/L); not recommended in pregnancy (safety not established); caution in breastfeeding (insufficient data)

ETHAMBUTOL: oral (relationship of dose to food doesn't matter) antitubercular and antileprotic; in WHO Model List of Essential Drugs; mode of elimination renal; bacteriostatic; impairs mycobacterial cell wall synthesis

Indications: *Mycobacterium* infections, tuberculous pneumonia (dosage 15-25 mg/kg daily)

Side Effects: retrobulbar neuritis (decreased visual acuity and red-green colour discrimination, central scotomata; very rare if dose $\leq$ 15 mg/kg/d, $\approx$ 5% if 25 mg/kg/d), peripheral neuritis with numbness and tingling of extremities (uncommon if normal renal function and dosage strictly observed), joint pain, gastrointestinal disturbances, malaise, headache, allergic reactions, rare anaphylaxis, hyperuricemia; modify dosage interval in renal dysfunction and in dialysis; safe in pregnancy and breastfeeding

Contraindications: children < 6 y; elderly patients; monitor breastfed infant for jaundice

ETHIONAMIDE

Indications: multibacillary leprosy when clofazimine totally unacceptable; *Mycobacterium* infections (dosage 0.75-1 g daily); tuberculosis prophylaxis

Side Effects: anorexia, nausea, vomiting, metallic taste, ganglionic blockade reactions (postural hypotension, depression), hepatotoxicity (especially in diabetics), severe allergic skin rash, purpura, gynecomastia, impotence, amenorrhoea, rare neurotoxicity

ISONIAZID (ISONICOTINIC ACID HYDRAZIDE, INAH, INH): oral (relationship of dose to food doesn't matter) antitubercular; no significant change in V_d or clearance in elderly; in WHO Model List of Essential Drugs; mode of elimination hepatic (renal); bactericidal; interferes with lipid and nucleic acid biosynthesis

Indications: hepatic granuloma; infections with *Mycobacterium tuberculosis* (spontaneous resistance $1:10^6$ organisms; dosage 300 mg daily or 15 mg/kg twice weekly), *Mycobacterium bovis*, *Mycobacterium kansasii*, *Mycobacterium szulgai*, *Mycobacterium xenopi*, *Mycobacterium avium-intracellulare*, *Mycobacterium leprae*, *Mycobacterium marinum, Mycobacterium gordonae, Mycobacterium malmoense;* tuberculosis prophylaxis; tuberculous pneumonia

Side Effects: peripheral neuritis (minimised with cotreatment with pyridoxine 25 mg orally daily), optic neuritis, hepatotoxicity ($\approx$ 0.3% in persons < 35 y, $\approx$ 2% in persons > 50 y; daily alcohol ingestion may be associated with higher incidence (and reduced effect of isoniazid)), pellagra-like syndrome, mental abnormalities, convulsions, epigastric distress, rare hypersensitivity, skin rash, nausea, mild abnormalities in liver function, subtle mood changes, single case reports of tinnitus and vestibular symptoms; decrease daily dose to 200 mg in severe renal insufficiency, administer routine pyridoxine supplement, monitor drug levels, treat toxicity with high dose pyridoxine and hemodialysis; reduce dose to ½ - 1/3 normal in liver dysfunction; dose adjustment required in dialysis; serum half life increased by para-aminosalicylic acid (particularly in rapid inactivators; reduced doses probably needed); additive effect on rifampicin reduction of plasma concentration of ketoconazole; marked increase in plasma level of carbamazepine, diazepam, phenytoin and disulfiram in some slow acetylators; may decrease plasma levels and effects of itraconazole, ketoconazole; decreased absorption by aluminium hydroxide gel; very weak association with oral contraceptive failure; safe in pregnancy

Contraindications: liver disease caused by other drugs; avoid if breastfeeding (if used, monitor infant for hepatitis, vision changes, fatigue, weakness, malaise, anorexia, nausea, vomiting and give pyridoxine to mother and infant)

RIFAMPICIN + ISONIAZID: in WHO Model List of Essential Drugs (essential that all combination tablets containing rifampicin shown to have adequate bioavailability)

Indications: infections due to *Mycobacterium tuberculosis*

Contraindications: pregnancy

ISONIAZID + THIOACETAZONE: in WHO Model List of Essential Drugs as complementary drug when drugs in main list cannot be made available and as drug for which adverse effects diminish benefit/risk ratio

Indications: tuberculosis

Side Effects: hypersensitivity, gastrointestinal symptoms, jaundice, peripheral neuritis; frequency of adverse reactions to thioacetazone appears much higher in tuberculosis patients infected with HIV than in those who are HIV negative
Contraindications: jaundice, liver disease caused by other drugs

PARA-AMINOSALICYLIC ACID (PAS)

Indications: infections with *Mycobacterium* (dosage 15-25 g daily)
Side Effects: gastrointestinal disturbances (nausea, gastric irritation, diarrhoea; extremely common), hypersensitivity (fever, rash, headache, sore throat), hepatotoxicity, blood dyscrasias, hmolytic anemia, allergic pulmonary reactions, bleeding tendencies, goitre, rare hypokalemia; serum levels increased by probenecid; increased risk of mutual toxicity when combined with salicylates (more likely in large doses); avoid in renal dysfunction

PYRAZINAMIDE: oral (relationship of dose to food doesn't matter) antitubercular; in WHO Model List of Essential Drugs; bactericidal; mechanism of action uncertain
Indications: treatment and prophylaxis of *Mycobacterium* infections (dosage 20-35 mg/kg/d) including tuberculous pneumonia
Side Effects: nausea and flushing common; less commonly, hepatotoxicity (large doses for prolonged periods; potentially lethal in combination with rifampicin), hyperuricemia, acute gout (rare; increased risk with allopurinol, colchicine, probenecid, sulfin pyrazone), non-gouty polyarthralgia, anorexia, vomiting, dysuria, malaise, fever, cutaneous hypersensitivity; rash; decreases cyclosporin levels; avoid in moderate to severe renal failure (glomerular filtration rate < 50 mL/min) and in dialysis
Contraindications: jaundice; avoid if pregnant (can be given after first trimester) or breastfeeding (insufficient data)

VIOMYCIN

Indications: mycobacterial bone marrow infections; mycobacterial hepatic granuloma; pulmonary tuberculosis and hepatitis due to *Mycobacterium avium-intracellulare*

CLOFAZIMINE: oral (take with or after food (absorption enhanced)) antileprotic and antitubercular; in WHO Model List of Essential Drugs
Indications: disseminated mycobacteriosis due to *Mycobacterium malmoense*; multibacillary leprosy; treatment of *Mycobacterium avium-intracellulare* infection
Side Effects: red-brown pigmentation of skin and, to lesser degree, conjunctiva, urine, sweat and sputum (may clear slowly when discontinued), nausea and diarrhoea with high dosage (crystals deposited in walls of small bowel and mesenteric lymph nodes), intestinal obstruction (occasional, dose-related), decreased sweating and tearing, giddiness, headache, blue-black discolouration of lesions, generalised retinal degeneration, corneal opacification
Contraindications: hepatic and renal impairment, pregnancy; avoid in breastfeeding if possible (may cause skin discolouration in infants)

DAPSONE: sulphone; oral (take with or after food) antileprotic; in WHO Model List of Essential Drugs
Indications: leprosy (including hepatitis); chronic mycobacterial ulcers
Side Effects: vomiting, nausea, anorexia, skin rashes, headache, insomnia, giddiness, tachycardia, haemolytic anaemia (more severe in those with glucose-6-phosphate dehydrogenase deficit), agranulocytosis, leucopenia, hepatitis, methaemoglobinemia (usually with high dosages), exfoliative dermatitis, peripheral neuropathy, cholestatic jaundice, infectious mononucleosis-like syndrome; dosage should be kept to a minimum; dosage modification not required in renal failure or in dialysis but monitor for myelosuppression; plasma levels increased by amprenavir, probenecid; bioavailability reduced by antacids and didanosine buffered formulations (space doses by 2-3 h); plasma levels reduced by rifabutin and rifampicin (increased risk of methemoglobinemia from rifampicin metabolite); very weak association with oral contraceptive failure
Contraindications: safety in pregnancy not established; avoid breastfeeding glucose-6-phosphate dehydrogenase deficient infants; monitor others for hemolysis and jaundice, especially if premature or < 1 mo

PROTHIONAMIDE

Indications: multibacillary leprosy when clofazimine totally unacceptable
Contraindications: careful use in cardiac and pulmonary disease, breast feeding; safety in pregnancy not established

ACETIC ACID

Indications: suppurative otitis media treatment and prophylaxis (topical); otitis externa (topical); toenail and web infections due to *Pseudomonas aeruginosa*

N-ACETYLCYSTEINE

Indications: bronchiectasis; bronchitis; cystic fibrosis
Side Effects: stomatitis, nausea, rhinorrhoea, very rare sensitivity, bronchospasm

ACI-JEL

Indications: vaginosis (topical)
Side-Effects: occasional local irritation and inflammation

AMMONIUM CHLORIDE

Indications: urine acidification

Side Effects: nausea and vomiting in large doses, acidosis and hypokalemia, hepatic encephalopathy with excessive doses

ANTITOXIN

Indications: infections with *Clostridium botulinum*, *Clostridium tetani*, *Corynebacterium diphtheriae*

ASCORBIC ACID

Indications: Chediak-Higashi syndrome; hyper-IgE-recurrent-infection syndrome; radiation-induced injury; repeated infections; surgical prophylaxis (postoperative); urinary acidification

ASPIRATION

Indications: septic arthritis due to *Salmonella*; bursitis; cat scratch disease; endophthalmitis; hepatic abscess

ASPIRIN (ACETYLSALICYLIC ACID)

Indications: reactive arthritis; mucocutaneous lymph node syndrome; rheumatic fever

Side Effects: may cause Reye syndrome in interaction with influenza A, influenza B, varicella-zoster and other viruses

BENZOYL PEROXIDE

Indications: mild to moderate acne vulgaris (topical)

Side Effects: allergic contact dermatitis and dryness

BETAMETHASONE

Indications: uveitis (topical)

Side Effects: hypersensitivity

BISMUTH FORMIC IODIDE

Indications: ischemic, varicose and decubitus ulcers (topical)

BISMUTH SUBSALICYLATE

Indications: dyspepsia; prevention of travellers' diarrhoea

Side Effects: chronic 'encephalopathy'

COLLOIDAL BISMUTH SUBCITRATE

Indications: gastric and duodenal ulcers and non-ulcer-related dyspepsia; simple gastritis; prophylaxis of traveller's diarrhoea

Side Effects: acute reversible renal failure with high dose/overuse, chronic 'encephalopathy' with prolonged high dose and renal impairment; impaired absorption of anticoagulants, digoxin, phenytoin, theophylline, hypoglycemics; serum level of theophylline decreased; absorption of oral iron impaired; antacids and H_2 antagonists interfere with action

BORIC ACID

Indications: suppurative otitis media (topical)

BROMHEXINE

Indications: bronchitis

Side Effects: occasional mild gastrointestinal, isolated instances of headache, vertigo, perspiration, skin rash

CARBENOXOLONE

Indications: aphthous mouth ulcers (topical)

CETRIMIDE

Indications: impetigo (topical)

CHLORHEXIDINE: in WHO Model List of Essential Drugs as antiseptic

Indications: burns prophylaxis (topical); pseudomonal folliculitis (topical); impetigo (topical); pericoronitis (topical); wound infections (topical)

Side Effects: occasional skin irritation, extremely rare generalised allergic reactions

CLIOQUINOL

Indications: 'swimmer's ear' (topical)

Side Effects: local irritation, hypersensitivity

COLONY-STIMULATING FACTORS

Indications: necrotising fasciitis due to *Pseudomonas aeruginosa*

CORTICOSTEROIDS

Indications: meningoencephalitis due to *Brucella*; *Streptococcus pneumoniae* infections

Contraindications: purulent conjunctivitis due to *Mycobacterium tuberculosis*

'CORYNEBACTERIUM PARVUM'

Indications: systemic infections prophylaxis in hyposplenism/splenectomy

DEXAMETHASONE

Indications: croup; endophthalmitis; enteric fever (critically ill patient in shock); epiglottitis; postneonatal pyogenic meningitis; otitis externa (topical)

Side Effects: usually not significant at dosages and duration of therapy used for these indications

DEXTRANASE

Indications: streptococcal endocarditis

Dienoestrol

Indications: recurrent dysuria-frequency syndrome related to menopause

Side Effects: theoretical risk of adverse effects associated with estrogens

Dietary Restriction

Indications: acute diarrhoea and/or vomiting; diverticulitis

Drainage

Indications: septic arthritis; cervical fascial space infections; acute empyema; hordeolum; nocardiosis; parotitis and submandibular sialadenitis due to *Burkholderia pseudomallei*; perinephric abscess; peritonsillar abscess; streptococcal and meningococcal pneumonia; prostatic abscess; pulmonary abscess; local and generalised sepsis due to *Mycobacterium*, *Salmonella*, *Aeromonas*; mastitis and breast abscess (unresponsive acute and advanced chronic); nasal septal abscess; postseptal cellulitis; acute sinusitis due to *Pseudomonas aeruginosa*; thyroiditis; tooth abscess; *Vibrio* wound and soft tissue infection

Electrolyte Replacement

Indications: cholera

Excision

Indications: infections with *Corynebacterium pseudotuberculosis*, *Mycobacterium, Nocardia*

Flumethasone

Indications: 'swimmer's ear' (topical)

Side Effects: occasional local irritation, hypersensitivity

Gentian Violet (Methylrosaniline Chloride): antiinfective dermatological drug; in WHO Model List of Essential Drugs

Gramicidin: polypeptide; increases permeability of plasma membrane; used topically, often in combination with other antimicrobials

Indications: 'swimmer's ear'

Side Effects: rare hypersensitivity; pregnancy

Granulocyte Transfusions

Indications: systemic infection prophylaxis in granulocytopenia

Heparin

Indications: cervical fascial space infections; meningococcal postneonatal pyogenic meningitis

Side Effects: occasional allergy, thrombocytopenia

Hexachlorophene

Indications: methicillin resistant *Staphylococcus aureus* control (topical); prophylaxis of recurrent *Staphylococcus aureus* skin infections (topical)

Humidification

Indications: acute chest infections; acute tracheitis

Hydrocortisone

Indications: eczema and allergic dermatitis; hemorrhoids and proctitis (topical); meningococccal post-neonatal pyogenic meningitis with evidence of Waterhouse-Friderichsen syndrome

Side Effects: usually not significant at dosages and duration of therapy used in these indications

Hydrogen Peroxide

Indications: impetigo (topical); necrotising ulcerative gingivostomatitis (topical)

Hyperbaric Oxygen

Indications: clostridial cellulitis

Immunoglobulin

Indications: mucocutaneous lymph node syndrome; systemic infection prophylaxis in agammglobulinemia, granulocytopenia

Indomethacin

Indications: ankylosing spondylitis; reactive arthritis

Side Effects: causes neutropenia by myelosuppression

Interferon

Indications: systemic infection prophylaxis in cell-mediated immunity disorders

Side Effects: flu-like symptoms, fatigue, headache, myalgia, rigour/chills, malaise in nearly all patients; hematological, hepatic, cardiovascular and neurological toxicities with higher doses; single case report of tinnitus and hearing loss; safety in pregnancy not established; caution in breastfeeding (insufficient data but low transfer anticipated)

Interleukin 2

Indications: systemic infection prophylaxis in cell-mediated immunity disorders

Intravenous Fluid

Indications: dehydration in acute diarrhoea and/or vomiting, diverticulitis, emphysematous gastritis

Isotretinoin
Indications: severe acne vulgaris
Side Effects: severe local intolerance in 5%
Leucocyte Transfusions
Indications: infection and debilitation in cases involving malignancy, chemotherapy or organ transplantation with a documented chemotactic defect; necrotising fasciitis due to *Pseudomonas aeruginosa*
Lithium
Indications: selected patients with increased cyclic adenosine monophosphate
Local Heat
Indications: mild dacrocystitis, adenitis and canaliculitis; hordeolum; chronic ulcers due to *Mycobacterium ulcerans*
Magenta
Indications: paronychia (topical)
Mercurochrome
Indications: wound infections (topical)
Nonsteroidal Anti-inflammatory Drugs
Indications: burn infections; prostatitis and seminal vesiculitis due to *Mycobacterium avium-intracellulare*
Side Effects: may cause necrotising fasciitis if used in treating inflammatory cutaneous lesions
Omeprazole
Indications: simple gastritis, duodenal ulcer and peptic ulcer
Side Effects: possible blindness or reduced vision
Oxindanac
Indications: neonatal and postneonatal pyogenic meningitis
Oxygen
Indications: acute chest infections
Pentovis
Indications: recurrent dysuria-frequency syndrome related to menopause
Phenylbutazone
Indications: ankylosing spondylitis; reactive arthritis
Side Effects: causes neutropenia by myelosuppression
Phenylephrine
Indications: mild dacrocystitis, adenitis and canaliculitis (topical)
Side Effects: may precipitate latent glaucoma
Contraindications: thyrotoxicosis, hypertension, tachycardia, patients on β-blockers
Piroxicam: nonsteroidal anti-inflammatory drug
Indications: possible benefit in *Pseudomonas aeruginosa* chronic pulmonary infection in cystic fibrosis
Side Effects: gastrointestinal effects in 20%, dizziness in 4%, headache in 4%, oedema in 3%, skin rash in 2%, sedation/drowsiness in 2%, pruritis in 1%, stomatitis in 1%
Plasma
Indications: systemic infection prophylaxis in complement deficiency, granulocytopenia
Plasma Exchange
Indications: haemolytic uraemic syndrome
Povidone Iodine: topical; in WHO Model List of Essential Drugs, replacing iodine as topical antiseptic agent of choice
Side Effects: hypersensitivity
Indications: burns; catheter lubrication; conjunctivitis; pseudomonal folliculitis; gingivitis; impetigo; keratitis and iritis due to Gram positive bacteria; methicillin resistant *Staphylococcus aureus* control; otitis externa; suppurative otitis media; paronychia; pericoronitis; stomatitis; surgical prophylaxis (skin antisepsis, postoperative wound spraying, intestinal instillation and lavage); ischemic, varicose and decubitus ulcers
Prednisone Acetate + Phenylephrine
Indications: uveitis
Contraindications: bacterial, fungal or viral infections
Prednisolone
Indications: bacterial keratitis and iritis; tuberculous meningitis; nonspecific proctitis; cardiovascular syphilis and neurosyphilis; ulcerative colitis; ? tetanus
Side Effects: usually not significant in dosages and duration of therapy used in these indications
Prednisone
Indications: Epstein-Barr virus infection (impending airway obstruction, patients exhausted by generalised infection); Lyme disease (meningoencephalitis, heart block); myocarditis and pericarditis due to *Mycobacterium tuberculosis*

Side Effects: usually not significant in dosages and duration of therapy used in these indications

PROBENECID: potentiates penicillins and some cephalosporins

Indications: streptococccal endocarditis; *Neisseria gonorrhoeae* infections; chronic pulmonary infection due to *Haemophilus influenzae* or *Staphylococcus aureus* in cystic fibrosis; *Salmonella* carriers; syphilis in human immunodeficiency virus infected patients

Side Effects: headache, gastrointestinal symptoms, urinary frequency, hypersensitivity, sore gums, flushing, alopecia, dizziness, anemia (including hemolytic and aplastic), nephrotic syndrome, leucopenia, hepatic necrosis, exacerbation of gout and uric acid stones

PROCAINE HYDROCHLORIDE

Indications: acute epididymitis and epididymoorchitis

PROPAMIDINE ISETHIONATE

Indications: mild purulent conjunctivitis (topical)

PROSTAGLANDIN E_1

Indications: mucocutaneous lymph node syndrome

Side Effects: fever in 14%, flushing in 10%, bradycardia in 7%, hypotension in 4%, seizures in 4%, tachycardia in 3%, diarrhoea in 3%, sepsis in 2%, cardiac arrest in 1%, oedema in 1%, disseminated intravascular coagulation in 1%, hypokalemia in 1%; apnea in 12% of neonates

PYRIDOXINE

Indications: prevention of peripheral neuritis in treatment with isoniazid; tetanus

Side Effects: interacts with L-dopa

PSYLLIUM HYDROPHILIC MUCILLOID

Indications: diverticulitis prophylaxis

REHYDRATION

Indications: cholera; acute diarrhoea and/or vomiting; parotitis and submandibular sialadenitis; toxic shock syndrome

SACCHAROMYCES BOULARDII

Indications: prophylaxis of antibiotic-associated diarrhoea and pseudomembranous colitis

Side Effects: fungemia in critically ill patients

SELENIUM SULPHIDE

Indications: seborrhoeic blepharitis (topical)

SILVER NITRATE: in WHO Model List of Essential Drugs as antiinfective ophthalmological agent

Indications: prophylaxis of gonococcal ophthalmia neonatorum (topical); rash due to *Pseudomonas aeruginosa*, *Yersinia* (topical)

SODIUM BICARBONATE

Indications: alkalinisation in treatment with sulphadiazine; seborrhoeic blepharitis (topical); geographic tongue, hairy tongue and black hairy tongue (mouthwash); mouth ulcers (mouthwash)

SODIUM CHLORIDE

Indications: geographic tongue, hairy tongue and black hairy tongue (mouthwash); mouth ulcers (mouthwash); pericoronitis (mouthwash); acute viral throat infections (gargle)

SODIUM CROMOGLYCATE

Indications: allergy

SODIUM DEOXYCHOLATE

Indications: prophylaxis of necrotising enterocolitis

SODIUM HYPOCHLORITE: in WHO Model List of Essential Drugs

Indications: wound infections (topical)

SURGERY

Indications: appendicitis; septic arthritis; brain and epidural abscess; bursitis; carpal tunnel syndrome; cholangitis and cholecystitis; diverticulitis; chronic empyema; endocarditis (patient with prosthetic valve; due to *Brucella*; where appropriate therapy fails to control infection; refractory congestive cardiac failure); endophthalmitis; false aneurism; mastoiditis; mesenteric lymphadenitis; mycotic aneurism; myonecrosis; necrotising enterocolitis; necrotising fasciitis; osteomyelitis and osteochondritis; pancreatic abscess; perianal and perinatal abscess and cellulitis in patients with malignant disease (unresponsive); pneumonitis due to *Corynebacterium equi;* psoas abscess; pulmonary abscess; rhinoscleroma; chronic sinusitis; splenic abscess; granulomatous synovitis; tenosynovitis; tooth abscess; mycobacterial chronic ulcers

TRIAMCINOLONE

Indications: 'swimmer's ear' (topical)

Side Effects: infrequent local adverse reactions, may damage collagen of tympanic membrane, may delay healing, systemic absorption may occur

TRICLOSAN: topical

Indications: mild acne vulgaris; methicillin resistant *Staphylococcus aureus* control; prophylaxis of recurrent *Staphylococcus aureus* skin infections

Side Effects: occasional redness/drying

TRANSFER FACTOR

Indications: hyper-IgE-recurrent infection syndrome; systemic infection prophylaxis in cell-mediated immunity disorders

VITAMIN E

Indications: deficiency of glutathione synthetase

ZINC

Indications: acrodermatitis enteropathica; Downs syndrome; leprosy

ZINC SULPHATE

Indications: mild dacrocystitis, adenitis and canaliculitis (topical)

DIPHENOXYLATE HYDROCHLORIDE: antimotility drug used in diarrhoea but no evidence that it alters the course of acute diarrhoea or that it diminishes the losses of fluids; CNS toxicity may occur in therapeutic dosages and bacillary dysentery may be aggravated

LOPERAMIDE: antimotility drug used in diarrhoea but no evidence that it diminishes losses of fluids or electrolytes when administered in conventional dosages; adverse effects on CNS have been observed in therapeutic dosages; paralytic ileus has been associated with its use in infants and children

KAOLIN AND PECTIN: absorbents used in diarrhoea but induce only a slight change in stool consistency; no evidence that they reduce the duration or severity of the diarrhoeal episode or that they reduce the losses of fluids or electrolytes; may interfere with antibiotic treatment when indicated

ACTIVATED CHARCOAL: absorbent used in diarrhoea but no evidence that it shortens the duration of diarrhoea or that it reduces the number or volume of stools; as an absorbent, it can bind antibiotics or enzymes

ATTAPULGITE AND SMEETITE: absorbents used in diarrhoea but no evidence that they have any effect on the losses of fluids and electrolytes; may bind or inactivate other drugs

Antifungals

FLUCYTOSINE (5-FLUOROCYTOSINE, 5-FC): in WHO Model list of Essential Drugs as complementary drug when drugs in main list are known to be ineffective or inappropriate for a given individual and as drug with limited applications or narrow spectrum of activity; oral (take with or after food; not registered in Australia) and parenteral; mode of elimination renal

Indications: mainly used in synergistic combination with amphotericin B against *Cryptococcus neoformans* (including cryptococcal meningitis); also severe *Aspergillus* infections; fungal brain and epidural abscess; *Candida* empyema, fungemia, chronic mucocutaneous infection, pneumonitis; chromoblastomycosis; disseminated *Dipodascus capitatus* and *Trichosporon beigelii* infections; eumycetoma; *Histoplasma capsulatum* infections; fungal meningitis; *Mucor* infections; fungal osteomyelitis and osteochondritis; fungal peritonitis; fungal pneumonia (including diffuse interstitial); fungal postseptal cellulitis; fungal prostatitis and seminal vesiculitis; chronic fungal sinusitis; systemic *Dipodascus capitatus*, *Exophiala dermatitidis* and *Pseudallescheria boydii* infections; torulopsosis; fungal urinary infections; mild zygomycosis

Side Effects: bone marrow toxicity (most commonly thrombocytopenia with high serum levels; monitoring advised; leucopoenia also common; agranulocytosis rare), hepatic toxicity (elevated liver enzymes common; hepatic necrosis rare); nausea, vomiting, diarrhoea, aaemia, rash common; gastrointestinal hemorrhage, allergic reactions, epidermal necrolysis, convulsions, myocardial toxicity, ventricular dysfunction rare; dosage adjustment necessary in renal insufficiency (monitor serum levels, monitor peripheral blood count (neutropenia, thrombocytopenia), gastrointestinal tonus) and in dialysis; may falsely elevate serum creatinine measurement by certain assays; safety in pregnancy not established; toxic level $>$ 100 mg/L peak; amphotericin and other drugs that predictably reduce glomerular filtration rate produce accumulation of flucytosine; increased risk of neutropenia $\pm$ thrombopenia with cytotoxic agents; cytarabine may antagonise antifungal activity

Contraindications: avoid if pregnant or breastfeeding (insufficient data)

KETOCONAZOLE: imidazole; oral (variable, acid-dependent absorption, increased if taken with acidic drinks and food); in WHO Model List of Essential Drugs as drug for which specific expertise, diagnostic precision or special equipment required for proper use; mode of elimination hepatic, not significantly excreted in urine; active against *Ajellomyces dermatitidis, Candida albicans*, *Candida krusei*, *Coccidioides immitis, Cryptococcus,* some strains of *Fusarium, Histoplasma, Paracoccidioides, Pseudallescheria boydii, Sporothrix schenckii, Trichosporon;* inactive against *Aspergillus, Candida tropicalis, Candida glabrata*; usual dose 200-400 mg; peak serum concentration 1.7-3.6 mg/L; half life 8 h; protein binding 99%; CSF/serum concentration $<$ 10; 50% absorption; 2% active drug in urine

Indications: first choice in blastomycosis (mild cases), chronic mucocutaneous candidiasis, nondisseminated extracutaneous coccidioidomycosis in immunocompetent host, entomophthoromycoses, histoplasmosis (nondisseminated extracutaneous disease in immunocompetent host), paracoccidioidomycosis, mild penicillosis, *Pseudallescheria boydii* infections and sporotrichosis; alternative in candidal esophagitis, onchyomycosis, severe oropharyngeal candidiasis, chronic or unresponsive candidal paronychia, pityrosporosis, superficial mycoses (dermatophytosis (unresponsive tinea corporis, pedis and cruris, tinea capitis, tinea unguium), vaginitis (recalcitrant and recurrent candidal, due to *Candida glabrata*, *Saccharomyces cerevisiae*)) when intolerance or failure with classical treatment; in nonimmunosuppressed patients, alternative to amphotericin B in systemic mycoses (eg., treatment and prophylaxis of systemic candidiasis (including pneumonitis), coccidioidomycosis (including diffuse interstitial pneumonia, mild to moderate stable disease of bones, genitourinary tract, peritonitis, viscera), *Exophiala dermatitidis*, systemic protothecosis); in immunosuppressed patients, no evidence of efficacy of treatment in curing infection except in treatment of esophagitis in granulocytopenia, but useful as prophylaxis against aspergillosis and candidiasis in chronic granulomatous disease and in cryptococcosis prophylaxis; also used in *Aspergillus* and *Mucor* infections, chromoblastomycosis, eumycetoma, fungal endocarditis, zygomycosis, seborrhoeic dermatitis and dandruff (shampoo), tinea versicolor

Side Effects: nausea, vomiting, pruritis common; may cause serious hepatic disease (mild reactions (transient elevated transaminases) in 5-10%, serious injury (severe hepatotoxicity with hepatocellular damage) in 1 in 10 000 - 1 in 70 000; monitor liver function tests monthly); rash uncommon; blocks steroid synthesis and may cause adrenal suppression and adrenal crisis, and gynecomastia, azoospermia and loss of libido through reduction in testosterone levels; psychiatric reactions rare; single case report of tinnitus; dosage modification not required in renal dysfunction or in dialysis; safety in pregnancy not established; bioavailability reduced by antacids, cimetidine, didanosine buffered preparations (take ketoconazole 2 h before), H_2-receptor antagonists, proton pump inhibitors; significant interactions with many other drugs metabolised in liver: risk of cardiac arrhythmias due to high plasma levels of astemizole, cisapride and terfenadine (which have resulted in deaths), increased risk of myopathy with simvastatin (acute rhabdomyolysis and hepatotoxicity reported), atorvastatin, fluvastatin, pravastatin, increased sedative/amnesic effects with midazolam, triazolam, may increase plasma concentrations of alprazolam, buspirone, carbamazepine, cisapride (increased risk of QT prolongation), cyclosporin, methylprednisolone, nevirapine (with decrease in ketoconazole levels), sildenafil, warfarin, indinavir, saquinavir, enhances

anticoagulant effect of coumarin, decreases plasma concentrations of theophylline, may cause hypoglycemia in combination with oral antidiabetic agents, plasma levels remarkably reduced by cimetidine, isoniazid, phenytoin, rifabutin and rifampicin (80%; effect increased by isoniazid; rifabutin/rifampicin levels may increase or decrease), plasma levels and effects may be decreased by isoniazid, phenytoin, phenobarbitone, may decrease effect of amphotericin, lopinavir and ritonavir may increase plasma levels; very weak association with oral contraceptive failure; safety in pregnancy not established; caution in systemic treatment in breastfeeding (insufficient data)

MICONAZOLE: imidazole; interferes with production of ergosterols; i.v. and topical; in WHO Model List of Essential Drugs (topical); mode of elimination hepatic; active against *Ajellomyces dermatitidis*, *Candida albicans*, *Candida krusei*, *Candida tropicalis*, *Coccidioides immitis*, *Cryptococcus*, *Histoplasma*, *Paracoccidioides, Sporothrix schenckii*, possibly *Fusarium* and *Trichosporon;* usual dose 0.6-1.8 g; peak serum concentration 7.5-10 mg/L; half life 24 h; protein binding 90%; CSF/serum concentration < 10; 50% absorption; 1% active drug in urine; no longer available in US or Europe

Indications: cutaneous, oropharyngeal and vulvovaginal candidiasis (topical); dermatomycoses including paronychia (topical); paracoccidioidomycosis; phaeohyphomycosis (topical); pityriasis versicolor (topical); fungal pneumonia (including diffuse interstitial); candidal local and generalised sepsis

Side Effects: oral: may induce hyponatremia; dosage modification not required in renal dysfunction or in dialysis; topical safe in pregnancy and breastfeeding; enhances anticoagulant effect of warfarin; oral hypoglycemics, cyclosporin, phenytoin, phenobarbitone increase serum levels (monitor or reduce dose if necessary); isoniazid, rifampicin, carbamazepine, phenytoin may reduce levels by increasing metabolism; topical: infrequent burning, stinging, itching, redness, rare allergic reactions

ECONAZOLE: imidazole

Indications: cutaneous candidiasis (topical); candidal otitis externa (topical); paronychia (topical); dermatophytosis; tinea versicolor

Side Effects: burning and pruritis in 3%; safe in pregnancy and breastfeeding; enhanced anticoagulant effect of warfarin

CLOTRIMAZOLE: imidazole; interferes with production of ergosterols

Indications: candidiasis in AIDS patients with CD4+ > 100; chronic mucocutaneous and vaginal candidiasis (gynaecology patients); candidal balanitis (topical); candidal oesophagitis (100% response); prophylaxis of oropharyngeal candidiasis in immunosuppressed patients; candidal otitis externa (topical); dermatomycoses including paronychia (topical); oesophagitis in granulocytopenia; pityriasis (tinea) versicolor (topical); vaginitis due to *Candida glabrata*, *Saccharomyces cerevisiae* (topical)

Side Effects: topical safe in pregnancy and brestfeeding, infrequent burning, stinging, itching, redness, rare allergic reactions

BIFONAZOLE: imidazole; active against dermatophytes, *Malassezia furfur* and *Candida*; safety in pregnancy not established

Indications: mucocutaneous candidiasis, dermatophytosis, tinea versicolor

FLUCONAZOLE: triazole; good tissue penetration, including CNS; well absorbed following oral administration (relationship of dose to food doesn't matter); relatively expensive; i.v. and oral; usual dose 100-400 mg; peak serum concentration 2.5-6.7 mg/L; half life 20-30 h; protein binding 11%; CSF/serum concentration > 60; excretion renal; 85% absorption; 66% active drug in urine; active against *Candida albicans*, *Candida tropicalis*, *Coccidioides immitis*, *Cryptococcus*, *Histoplasma*, *Paracoccidioides, Sporothrix schenckii*, *Trichosporon*, *? Ajellomyces dermatitidis,* ? *Pseudallescheria boydii;* variable activity against *Fusarium*; inactive against *Aspergillus*, *Issatchenkia orientalis*, *Candida glabrata*

Indications: chronic mucocutaneous candidiasis in AIDS (CD4+ > 100); treatment and prophylaxis of systemic candidiasis; mild to moderate coccidioidomycosis of bones, genitourinary tract, peritonitis, viscera; cryptococcosis (induction, maintenance, prophylaxis); fungal endocarditis; less severe fungal endophthalmitis; fungemia; meningitis (cryptococcal; induction in mild and maintenance in coccidioidal); candidal esophagitis (85% response); severe oropharyngeal candidiasis in immunocompromised and when failure of response to other treatment; systemic *Exophiala dermatitidis* and *Pseudallescheria boydii* infections; fungal urinary infections; recalcitrant candidal vaginitis

Side Effects: nausea (4% in AIDS), headache (2% in AIDS), skin rash (2% in AIDS), abdominal pain (2% in AIDS), vomiting (2% in AIDS), diarrhoea (2% in AIDS); pruritis, constipation common; asymptomatic liver function tests elevations in 1-2%; renal complications in renal dysfunction; serious adverse blood events (thrombocytopenia, neutropenia, leucopenia) 2.8/100,000 prescriptions; hypokalemia, hepatitis, peripheral neuropathy, adrenal suppression uncommon; alopecia, allergy rare; dose interval adjustment required in renal failure and in dialysis; increased risk of QT prolongation with cisapride; may increase plasma levels and effects of clarithromycin, cyclosporin, glibencamide, glipizide, phenytoin, rifabutin (may cause uveitis), theophylline, warfarin; bioavailability reduced by rifampicin; possible interaction with astemizole and terfenadine; very weak association with oral contraceptive failure; safe in breastfeeding

Contraindications: pregnancy

ITRACONAZOLE: triazole; oral (capsules: take with or after food (absorption enhanced by food and acidic drinks, decreased by proton pump inhibitors or histamine H_2-receptor antagonists); oral solution: take 1 h before food); usual dose 200 mg; peak serum concentration 0.1 mg/L; half life 15-40 h; protein binding 99.8%; CSF/serum concentration < 10; excretion hepatic; 99% absorption; 1% active drug in urine; improved activity against filamentous fungi, eg. *Aspergillus*; also active against

Ajellomyces dermatitidis, *Candida albicans*, *Candida tropicalis*, *Issatchenkia orientalis*, *Cryptococcus*, *Histoplasma*, *Paracoccoidoides*, *Sporothrix schenckii*, *Trichosporon*, ? *Pseudallescheria boydii*; variable activity against *Fusarium*
Indications: mild or moderate systemic aspergillosis; mild cases of blastomycosis; oesophageal and oropharyngeal candidiasis; chromoblastomycosis; mild to moderate stable coccidioidomycosis of bones, genitourinary tract, peritonitis, viscera; less severe fungal endophthalmitis; histoplasmosis (induction and maintenance); fungal meningoencephalitis; myocarditis and pericarditis due to *Aspergillus*; candidal esophagitis (71% response); oropharyngeal candidiasis in immunosuppressed; fungal osteomyelitis and osteochondritis; malignant otitis externa due to *Aspergillus*; fungal pneumonia; penicilliosis (mild, maintenance); scedosporiosis; local and generalised sepsis due to *Alternaria;* sporotrichosis (cutaneous lymphatic, maintenance)
Side Effects: asymptomatic liver function tests elevations in 2-3%; serious liver problems, some resulting in transplantation or death, reported; single case report of vestibular symptoms; others as for **FLUCONAZOLE**; increased sedative/amnesic effects with alprazolam, oral midazolam, triazolam; may increase plasma levels and effects of astemizole, cisapride (increased risk of QT prolongation) and terfenadine (risk of cardiac arrhythmias, which have resulted in deaths), buspirone, cyclosporin, digoxin, felodipine, indinavir, nifedipine, norethisterone, oral hypoglycemics, prednisolone, quinidine, saquinavir, sildenafil, vincristine, warfarin; plasma levels and effects may be decreased by amphotericin (amphotericin may also not be as effective; may be antagonistic), carbamazepine, isoniazid, phenytoin, phenobarbitone, rifabutin and rifampicin; bioavailability reduced by antacids, didanosine buffered formulations (take itraconazole 2 h before), H_2-receptor antagonists and proton pump inhibitors; increased risk of myopathy with simvastatin (acute rhabdomyolysis and hepatotoxicity reported), atorvastatin, fluvastatin, pravastatin; reduces clearance of busulphan; levels almost doubled by clarithromycin; plasma levels increased by amprenavir, lopinavir, ritonavir; very weak association with oral contraceptive failure; dosage modification not required in renal failure or in dialysis; safety in pregnancy and breastfeeding not established
VORICONAZOLE: triazole; structurally related to fluconazole; spectrum similar to itraconazole; tablets (take 1 h before or 1 h after food), powder for injection
Indications: invasive aspergillosis, serious infections with *Candida, Scedosporium, Fusarium*
Side Effects: as for **FLUCONAZOLE** + common transient visual changes (in 30%) and hallucinations and uncommon hepatotoxicity (including fatal liver failure), Stevens-Johnson syndrome; increased plasma levels of alprazolam, midazolam, triazolam may lead to prolonged sedation; may increase plasma levels of atorvastatin, simvastatin; likely enhanced warfarin effect; safety in pregnancy not established
Contraindications: coadministration with carbamazepine, ergotamine, pimozide, cisapride; avoid in breastfeeding (insufficietn data)
CASPOFUNGIN: echniocandin; inhibits β-(1,3)-D-glucan in cell wall; slow i.v. infusion
Indications: salvage therapy in invasive aspergillosis; *Candida* esophagitis and candidemia
Side Effects: nausea, vomiting, fever, flushing, pain or redness or phlebitis at site of infusion, decrease in haemoglobin, increase in liver enzyme concentrations common; anaphylaxis rare; cyclosporin increases levels; decreases tacrolimus levels; plasma levels reduced by catbamazepine, dexamethasone, efavirenz, nelfinavir, nevirapine, phenytoin, rifampicin
Contraindications: concomitant cyclosporin
CICLOPIROXOLAMINE
Indications: oral: more serious fungal infections; topical: tinea pedis
GRISEOFULVIN: fungistatic; inhibits dermatophyte invasion of keratin structures; effective orally (take with or after food (absorption enhanced)) but has to be taken for prolonged periods; may also be effective topically; in WHO Model List of Essential Drugs as drug for which adverse effects diminish benefit/risk ratio
Indications: kerion; recalcitrant tinea due to *Microsporum, Trichophyton, Epidermiphyton;* unresponsive tinea corporis, pedis and cruris; tinea capitis; tinea unguium
Side Effects: headache, dry mouth, nausea, vomiting common; neuritic pains, arthralgia, mental confusion, diminished motor coordination (doses > 1 g daily), skin sensitivity reactions, urticaria, photosensitivity, petechial rash, exacerbation and/or precipitation of lupus erythematosus, fixed drug eruption, blurred vision, paraesthesia, myelosuppression, menstrual irregularities uncommon; hepatic toxicity, epidermal necrolysis rare; ? precipitates acute attacks in porphyria, ? intolerance of alcohol (tachycardia, flush); unpredictable marked decrease in effect of warfarin due to induction of metabolism; absorption impaired by phenobarbitone; dose adjustment not required in renal failure or in dialysis; safety in pregnancy not established; very weak association with contraceptive failure
Contraindications: liver failure, porphyria; avoid if breastfeeding (insufficient data)
AMPHOTERICIN B: polyene; oral (take with or after food) and parenteral; fungistatic and fungicidal in high concentrations; decreased fungicidal effect under anaerobic conditions; in WHO Model List of Essential Drugs; liposomal and lipid formulations less toxic but much more expensive
Indications: treatment of choice for most serious systemic fungal infections; consultation with infectious disease physician or clinical microbiologist advised; invasive severe aspergillosis (including arteritis, burn infections, myocarditis and pericarditis, skin lesions, upper airways, rhinosinusitis prophylaxis in neutropenics (nasal spray)); systemic *Bipolaris*

infections; blastomycosis (including splenic abscess); disseminated and systemic *dipodascus capitatus* infection; fungal brain and epidural abscess; candidiasis (bronchopulmonary, chronic mucocutaneous, myocarditis and pericarditis, resistant oesophagitis, mild oropharyngeal (topical)); fungal cellulitis; fungal chorioretinitis; chromoblastomycosis; disseminated coccidioidomycosis; cryptococcosis treatment (including pancreatitis and pulmonary); empiric therapy in neutropenia, AIDS and acute myelogenous leukemia patients; chronic fungal empyema; fungal endocarditis; systemic *Exophiala dermatitidis* infection; severe fungal endophthalmitis; eumycetoma; fungemia; fungal genitourinary infections; geotrichosis; systemic *Hansenula* infections; fungal hepatic granuloma; fungal hepatitis; histoplasmosis (anterior uveitis, bone marrow infection, disseminated, oronasopharyngeal, induction of treatment in severe); meningitis (candidal, coccidioidal, cryptococcal); mucormycosis; oesophagitis in granulocytopenics; ophthalmic mycoses; fungal osteomyelitis and osteochondritis; paracoccidioidomycosis; severe penicilliosis; fungal peritonitis; phaeohyphomycosis; fungal pneumonia (disseminated aspergillosis, blastomycosis, coccidioidomycosis, pulmonary cryptococcosis, pulmonary histoplasmosis, diffuse interstitial pneumonia) and pneumonitis; fungal postseptal cellulitis; fungal prostatic abscess; fungal prostatitis and seminal vesiculitis; systemic protothecosis; invasive *Saccharomyces cerevisiae* infections; chronic fungal sinusitis; skin lesions due to *Drechslera*; disseminated and pulmonary sporotrichosis; tinea nigra; torulopsosis; disseminated *Trichosporon beijelii* infection; zygomycosis
Side Effects: minimised by alternate day therapy, 0.5-1 L 0.9% sodium chloride prior to infusion; hydrocortisone, antihistamines, antiemetics, opiates, antipyretic may provide symptomatic relief; i.v.: chills and fever (ameliorated by ibuprofen), nausea, vomiting, malaise, muscle and joint pain, hypotension (minimised by aspirin + antihistamine or 50 mg hydrocortisone), local thrombophlebitis (1000 U heparin added to infusion may be helpful), anaemia (normocytic normochromic), nephrotoxicity (in 80%; not with methyl ester; lower incidence with lipid complex or liposomal; dose dependent and largely reversible; decreased creatinine clearance, isothenuria, decreased excretion of H^+, abnormal urine sediment, renal tubular, acidosis, nephrocalcinosis, probable increased risk in renal insufficiency (avoid use unless absolutely indicated, monitor renal function); increased risk with aciclovir, aminoglycosides, cyclosporin, frusemide, vancomycin) common; urinary retention, anuria, oliguria, malignant hypertension, cardiac arrest, unusual arrhythmias, blood dyscrasias, gastrointestinal bleeding, rash, neurological effects, acute hepatic failure, jaundice and hepatocellular dysfunction (methyl ester), headache uncommon; hypersensitivity reactions, hypokalemia (may increase risk of digoxin toxicity), hypomagnesia, severe loss of body weight (not with methyl ester), hearing loss, anaphylaxis, bronchiolitis obliterans rare; intrathecal: pain along distribution of lumbar nerves, paresthesias, nerve palsies (foot drop), chemical meningitis, ? impaired vision, red man syndrome, topical: pruritis, burning in intertriginous areas, rare sensitisation; oral: diarrhoea; liposomal: cardiopulmonary toxicity; causes neutropenia by myelosuppression; toxic level > 2 μmol/L (1.5 mg/L); increases nephrotoxicity of cyclosporine; miconazole may antagonise antifungal activity; plasma levels decreased by phenobarbitone; may significantly reduce warfarin activity; probably safe in pregnancy; dose adjustment not needed in renal failure or in dialysis
Contraindications: avoid i.v. in breastfeeding (insufficient data)

NYSTATIN: polyene; fungistatic and fungicidal in high concentrations; poorly absorbed from gastrointestinal tract (timing to food does not matter); not absorbed through skin or mucous membranes; creams, gels, vaginal pessaries, lozenges, tablets
Indications: bronchopulmonary candidiasis (aerosol); cutaneous candidiasis (topical); oropharyngeal candidiasis (lozenge); paronychia (topical); 'swimmer's ear' (topical); systemic infection prophylaxis in cell-mediated immunity disorders, granulocytopenia; candidal vaginitis (topical; gynaecology and obstetric patients and male partners)
Side Effects: nausea, vomiting, diarrhoea; safe in pregnancy and breastfeeding

TERBINAFINE: allylamine; interferes with the production of ergosterols; fungicidal for many dermatophytes; oral (well absorbed from gut; relationship of dose to food doesn't matter) and topical (73% efficacy in tinea pedis)
Indications: unresponsive tinea corporis, pedis and cruris; tinea unguium
Side Effects: oral: gastrointestinal effects (abdominal pain, nausea), mild allergic skin reactions, taste disturbances including loss of taste, transient elevated transaminases common; toxic epidermal neurolysis, hepatitis, neutropenia, Stevens-Johnson syndrome rare; isolated cases of hepatobiliary dysfunction, cholestatic jaundice, dizziness, tiredness, sedation, light-headedness, chest pain; asymptomatic liver function tests elevations in 1-2%; serious liver problems, some resulting in transplantation or death, reported; probably safe in pregnancy; dose adjustment required in renal failure, not in dialysis; rifampicin and other enzyme inducing agents may decrease levels and effects; cimetidine may block metabolism, increasing plasma levels; topical: redness, itchiness, stinging, some reports of menstrual disorders in women taking oral contraceptives, rare allergic reactions
Contraindications: avoid if breastfeeding (insufficient data); caution in hepatic disease

UNDECENOIC ACID
Indications: tinea pedis (67% efficacy)

TOLNAFTATE
Indications: tinea pedis (74% efficacy)

AMOROLFINE: morpholine
Indications: tinea unguium (nail lacquer)
Side Effects: safety in pregnancy not established

Pentamidine Isethionate: mechanism of action poorly understood; in WHO Model List of Essential Drugs as main list drug to improve compliance

Indications: pneumocystosis treatment and prophylaxis

Side Effects: i.v.: immediate hypotension, nausea and vomiting; later, local pain at injection site, abscess formation, neutropenia (frequent in AIDS), thrombocytopenia, rash (rare), nephrotoxicity (mild azotemia to severe tubular necrosis; increased risk (including acute renal failure) with amphotericin, cidofovir, foscarnet), hepatitis with abnormal liver function tests, hypoglycemia and hyperglycemia, cardiotoxicity in 23% of patients treated for antimony-resistant kala azar, hypomagnesia, hypokalemia, acute pancreatitis, ventricular arrhythmias; severe hypocalcemia with foscarnet; possible potentiation of toxic effects on rapidly growing cells (bone marrow, spermatogonia, germinal layers of skin and gastrointestinal mucosa) with ganciclovir; increased risk of QT prolongation with all drugs prolonging QT interval; diabetes in 20% of patients treated for 3 weeks; dose adjustment required in renal failure, not in dialysis (except continuous venovenous or arteriovenous hemodialysis); aerosolised: bronchospasm, acute pancreatitis, mild hypoglycaemia, increased risk of spontaneous pneumothorax; safety in pregnancy not established

Dapsone

Indications: *Pneumocystis jiroveci* pneumonia prophylaxis in HIV positive that cannot tolerate cotrimoxazole

Side Effects: see Chapter 21

Trimethoprim-Dapsone

Indications: diffuse interstitial pneumonia due to *Pneumocystis jiroveci*

Side Effects: skin rash in 10%, nausea and vomiting in 7%, methaemoglobinemia in 3%, hemolytic anemia (particularly in patients with G6DP deficiency); safety in pregnancy not established

Pyrimethamine: selectively inhibits dihydrofolate reductase; half life 96 h; oral (take with or after food); in WHO Model List of Essential Drugs

Indications: infections with *Pneumocystis*; interstitial plasma cell pneumonia

Side Effects: anorexia, vomiting, folinic acid reversible megaloblastic anemia, usually reversible leucopenia and other hematological toxicity with long term use, may be embryopathic; additional suppression of folate metabolism with cotrimoxazole, sulphonamides, trimethoprim and other folate antagonists (including cytostatic drugs) may result in serious pancytopenia and megaloblastic anemia, rarely aplasia; convulsions in children with CNS leukemia treated with methotrexate; dose adjustment not required in renal failure or in dialysis but monitor for myelosuppression; safety in pregnancy not established; safe in breastfeeding

Pyrimethamine-Dapsone: interferes with folate metabolism; dapsone half life 21 hours

Indications: *Pneumocystis* prophylaxis

Side Effects: agranulocytosis, cyanosis, allergic dermatitis, gastrointestinal disorders, acute hemolysis in individuals with glucose-6-phosphate dehydrogenase deficiency; safety in pregnancy not established

Contraindications: avoid if breastfeeding G6PD deficient infants; monitor for hemolysis and jaundice if breastfeeding premature infant or < 1 mo old; avoid high doses if breastfeeding any infant (may interfere with folic acid metabolism)

Pyrimethamine-Sulphadoxine: interferes with folate metabolism; in WHO Model List of Essential Drugs as complementary drug for curative treatment of malaria when drugs in main list are known to be ineffective or inappropriate for a given individual; half life sulphadoxine 200 h; take with or after food

Indications: prophylaxis of diffuse interstitial pneumonia due to *Pneumocystis jiroveci*

Side Effects: erythema multiforme, orogenital lesions, pharyngitis, pruritis, rash, agranulocytosis, exfoliative dermatitis, serum reaction type reaction, urticaria, gastrointestinal disturbances, induction of folate deficiency; Stevens-Johnson syndrome (can be fatal), toxic epidermal necrolysis rare; much more common when taken in combination with chloroquine

Contraindications: pregnancy; neonatal period; avoid if breastfeeding premature infant or infant < 1 mo or with G6PD deficiency

Pyrimethamine-Sulphadiazine

Indications: *Pneumocystis* prophylaxis

Side Effects: seen in 30-45% of patients; severe skin rash, leucopoenia, thrombocytopenia, elevated levels of serum transaminases, bone marrow toxicity, pancytopenia, megaloblastic anaemia

Clindamycin

Indications: diffuse interstitial pneumonia due to *Pneumocystis jiroveci*

Side Effects: see Chapter 21

Primaquine: oral (take with or after food)

Indications: infections with *Pneumocystis jiroveci*

Side Effects: abdominal cramps and pain, epigastric distress, nausea and vomiting on an empty stomach common; hemolytic anemia with large doses and in those with glucose-6-phosphate dehydrogenase deficiency, methemoglobinemia and cyanosis uncommon; cardiac arrhythmias, hypertension, anemia, leucopenia, agranulocytosis, fever, rash rare; risk of toxicity increased by quinacrine; increases plasma levels and adverse effects of mefloquine

Contraindications: pregnancy, glucose-6-phosphate dehydrogenase deficiency (including breastfed infants; monitor also for haemolysis and jaundice in breastfed premature infants and those < 1 mo)
ATOVAQUONE: take with or after food (absorption enhanced); absorption reduced in patients with severe diarrhoea; plasma levels significantly reduced by metoclopramide, rifampicin
Indications: *Pneumocystis jiroveci* infections in patients unable to tolerate other agents
Side Effects: occasional rash, fever, elevated liver function tests, abdominal pain, vomiting, nausea, diarrhoea, anorexia, headache, dizziness, myalgia; probably safe in regnancy
Contraindications: avoid in breastfeeding (insufficient data)
CARBUTAMIDE
Indications: *Pneumocystis jiroveci* infections
EFLORNITHINE: in WHO Model List of Essential Drugs as complementary drug for use in rare disorders or in exceptional circumstances
Indications: diffuse interstitial pneumonia due to *Pneumocystis jiroveci*
TRIMETREXATE-LEUCOVORIN
Indications: diffuse interstitial pneumonia due to *Pneumocystis jiroveci*
Side Effects: bone marrow suppression (particularly neutropenia; alleviated by increasing dose of leucovorin)
CALCIUM FOLINATE
Indications: prevention of anemia in trimetrexate therapy
ZIDOVUDINE
Indications: prophylaxis of diffuse interstitial pneumonia due to *Pneumocystis jiroveci* in AIDS
Side Effects: see Chapter 20
FUMAGILLIN: not registered for use in Australia
Indications: microsporidial infections
Side Effects: thrombocytopenia, resolving on cessation of therapy, in immunocompromised patients
BENZOIC ACID + SALICYLIC ACID: antifungal dermatological drug; in WHO Model List of Essential Drugs
Indications: fungal skin infections (apply often)
Side Effects: may cause discomfort
BORIC ACID
Indications: otitis media due to *Aspergillus*; vaginitis due to *Saccharomyces cerevisiae*, *Candida glabrata*
CANDICIDIN
Indications: candidal vulvitis (topical)
COTRIMOXAZOLE
Indications: nondisseminated extracutaneous histoplasmosis in immunocompetent host; *Pneumocystis jiroveci* infections
Side Effects: see Chapter 21
DESENSITISATION
Indications: candidal vaginitis involving hypersensitisation
DEXAMETHASONE
Indications: severe fungal endophthalmitis
DIAMTHAZOLE: topical antifungal
Side Effects: irritation and sensitisation
DRAINAGE
Indications: candidal pancreatic abscess; perinephric abscess; prostatic abscess; chronic sinusitis
FENTICLOR: topical antifungal
Side Effects: photosensitivity
GENTIAN VIOLET (METHYLROSANILINE CHLORIDE): antiinfective dermatological drug; in WHO Model List of Essential Drugs
Indications: oropharyngeal candidiasis (topical)
GRANULOCYTE INFUSIONS
Indications: fusariosis; systemic *Exophiala dermatitidis* infection
GRANULOCYTE MACROPHAGE COLONY STIMULATORY FACTOR
Indications: fusariosis
HALOGENATED SALICYLANILIDES: topical antifungal
Side Effects: photosensitivity
HYPERBARIC OXYGEN
Indications: zygomycosis
HYDROCORTISONE
Indications: induction of treatment in severe coccidioidal meningitis

HYDROXYQUINOLINES: topical antifungal
Side Effects: irritation and sensitisation, yellow staining of fabrics
HYDROXYSTILBAMIDINE ISETHIONATE
Indications: blastomycosis if amphotericin B fails; cutaneous blastomycosis
INTERFERON-GAMMA
Indications: prophylaxis and treatment of pulmonary aspergillosis in chronic granulomatous disease
NATAMYCIN (PIMAFUCIN)
Indications: cutaneous, oral and vulvovaginal candidiasis (topical); fungal keratitis and iritis (topical); rhinosporidiosis
Side Effects: nausea, diarrhoea
POTASSIUM IODIDE: in WHO Model List of Essential Drugs
Indications: cutaneous-lymphatic sporotrichosis
Side Effects: gastrointestinal upset, metallic taste, rash
POVIDONE IODINE: in WHO Model List of Essential Drugs
Indications: *Rhizopus* isolated skin lesions
PREDNISOLONE
Indications: bagassosis and farmer's lung; hypoxia in early diffuse interstitial pneumonia due to *Pneumocystis jiroveci*
SELENIUM SULPHIDE: in WHO Model List of Essential Drugs as complementary drug for use in rare disorders or in exceptional circumstances
Indications: dandruff (shampoo); tinea versicolor (topical)
SHAVING
Indications: piedra; trichosis axillaris
SODIUM IODIDE
Indications: arteritis due to *Pythium*
SODIUM THIOSULPHATE: antifungal dermatological drug; in WHO Model List of Essential Drugs
Indications: tinea versicolor (topical)
STEROIDS
Indications: anterior uveitis due to *Histoplasma capsulatum*; fungal chorioretinitis
SULPHONAMIDES
Indications: paracoccidioidomycosis
Side Effects: see Chapter 21
SULPHUR
Indications: erythrasma; piedra; trichosis axillaris
SURGERY
Indications: fungal arteritis; brain abscess due to *Bipolaris*, *Rhinocladiella atrovirens; Aspergillus* burn infections; chromoblastomycosis; severe or potentially severe coccidioidomycosis of bones, genitourinary tract, peritonitis, viscera; cutaneous histoplasmosis; fungal endocarditis; epidural abscess; fusariosis; fungal keratitis and iritis; fungal meningoencephalitis; candidal myocarditis and pericarditis; phaeohyphomycosis; fungal pneumonia (localised pulmonary aspergillosis, extensive pleural disease); fungal prostatitis; scedosporiosis; local and generalised sepsis due to *Alternaria*, *Aspergillus*; skin lesions due to *Drechslera*, *Rhizopus*; splenic abscess; sporotrichosis; systemic *Exophiala dermatitidis* infection; zygomycosis
THIABENDAZOLE
Indications: chromoblastomycosis
Side Effects: see Chapter 23
TOPICAL DRY HEAT
Indications: phaeohyphomycosis
TRANSFER FACTOR
Indications: chronic mucocutaneous candidiasis; candidal vaginitis in anergy; cryptococcal meningitis (investigational)

Chapter 23

Antiparasitic Agents

AMPHOTERICIN B: in WHO Model List of Essential Drugs
Indications: amoebic meningoencephalitis, visceral leishmaniasis
Side Effects: see Chapter 22
MICONAZOLE
Indications: amoebic meningoencephalitis
Side Effects: see Chapter 22
RIFAMPICIN
Indications: amoebic meningoencephalitis
Side Effects: see Chapter 21
CLOTRIMAZOLE
Indications: keratitis and iritis due to *Acanthamoeba* (topical); *Trichomonas vaginalis* infections (topical)
Side Effects: see Chapter 22
DIBROMOPROPAMIDINE ISETHIONATE
Indications: keratitis and iritis due to *Acanthamoeba* (topical)
GENTAMICIN
Indications: keratitis and iritis due to *Acanthamoeba* (topical)
NEOMYCIN
Indications: keratitis and iritis due to *Acanthamoeba* (topical)
Side Effects: sensitisation
PROPAMIDINE ISETHIONATE
Indications: keratitis and iritis due to *Acanthamoeba* (topical)
DEHYDROEMETINE
Indications: extraintestinal and symptomatic intestinal amoebiasis
DILOXANIDE FUROATE: luminal amoebicide; in WHO Model List of Essential Drugs; oral (take with or after food); available in US only from CDC; not available in Australia; poor GI absorption
Indications: infections with amoebae including *Entamoeba histolytica* (elimination of carrier state)
Side Effects: flatulence; diplopia (rare); dose adjustment not required in renal failure or in dialysis; safety in pregnancy or breastfeeding not established
EMETINE
Indications: symptomatic intestinal amoebiasis (effective for both luminal and invasive infections); hepatitis and hepatic abscess due to *Entamoeba histolytica* if no response to metronidazole in 72 h (prolonged treatment may be recommended)
Side Effects: unsafe because of drug accumulation and side effects, including cardiotoxicity and death
IODOQUINOL (DIODOHYDROXYQUINE): hydroxyquinolone; treatment course 20 d; effective and inexpensive
Indications: infections with amoebae including *Entamoeba histolytica* (elimination of carrier state); has not been shown to be effective for routine treatment of diarrhoea
Side Effects: associated with severe neurological disorders, optic neuritis and atrophy with extended use (rare)
METRONIDAZOLE: nitroimindazole; take with or after food (benzylmetronidazole: ½ - 1 h before food); in WHO Model List of Essential Drugs; spectrum includes amoebae (*Entamoeba histolytica*, *Giardia intestinalis, Trichomonas vaginalis*)
Indications: amoebiasis (cyst passers, extraintestinal (brain abscess, cutaneous, hepatic abscess), symptomatic intestinal; treatment of choice for invasive); biliary cirrhosis due to flukes; chronic diarrhoea; enteritis due to *Balantidium coli, Blastocystis hominis,* protozoans other than *Cryptosporidium*, *Isospora belli* and microsporidia; dracuculiasis; giardiasis; isolated skin lesions due to *Leishmania braziliensis, Leishmania mexicana;* trichomoniasis; Indian visceral leishmaniasis; trichomonal vulvovaginitis
Side Effects: see Chapter 21
TINIDAZOLE: nitroimidazole; take with or after food; as effective as metronidazole and better tolerated; not available in US
Indications: intestinal amoebiasis; enteritis due to protozoans other than *Cryptosporidium* and *Cystoisospora belli*; giardiasis; hepatic abscess due to *Entamoeba histolytica*; persistent traveller's diarrhoea; trichomonal vaginitis
Side Effects: see Chapter 21
ORMIDAZOLE: as for **TINIDAZOLE**
PAROMOMYCIN: aminoglycoside; treatment course 7 d

Indications: intestinal amoebiasis; enteritis due to *Balantidium coli*, *Diphyllobothrium*, *Hymenolepis, Taenia*; isolated skin lesions due to *Leishmania tropica;* giardiasis; visceral leishmaniasis; not registered for use in Australia
Side Effects: gastrointestinal disturbances, nephrotoxicity and ototoxicity (rare); may be used during pregnancy
CHLOROQUINE: rapidly acting blood schizonticide; effective against *Plasmodium malariae, Plasmodium ovale* and *Plasmodium vivax* but widespread resistance of *Plasmodium falciparum*; phosphate (preferred form) and sulphate oral preparations (take with or after food), hydrochloride for i.v. and i.m. use; in WHO Model List of Essential Drugs as main list drug for curative treatment and prophylaxis of malaria and as complementary drug in amoebiasis (liver abscess only, not effective against luminal parasites) when drugs in the main list are known to be ineffective or inappropriate for a given individual; half life 120 h; high GI absorption
Indications: amoebic liver abscess if no response to metronidazole in 72 h; babesiosis; cholangitis and cholecystitis due to *Clonorchis sinensis*, *Opisthorchis*; infections with *Leishmania*; treatment and prophylaxis of malaria
Side Effects: headache, gastrointestinal upset (nausea, vomiting, diarrhoea; can be minimised by administering with meals), pruritis, lichenoid skin eruptions common; anxiety, personality changes, psychosis, reversible corneal deposits (minute subepithelial spots or cat's whiskers radiation) and retinopathy (membranous or myeloid bodies in ganglion cells) on prolonged administration (> 100 g; particularly fair-skinned, blue-eyed people), blurring of vision due to problems of visual accommodation in long term use uncommon; myopathy, worsening of psoriasis, tinnitus, ototoxicity (hearing loss) with long term use, photosensitivity, TSH elevation, exacerbation of symptoms of porphyria, provocation of seizures in people with epilepsy, alopecia, bleaching of hair, mucous membrane pigmentation, irreversible renal injury rare; overdose → cardiovascular collapse and death (particularly with i.v. and i.m.); must never be given by i.v. bolus injection; dose adjustment required in severe renal failure (glomerular filtration rate < 10 mL/ min), not in dialysis except in continuous venovenous or arteriovenous hemodialysis; weekly dosing safe in pregnancy; absorption moderately reduced by antacids; increases plasma levels of chlorpromazine (increased risk of QT interval prolongation), cyclosporin (possible nephrotoxicity), digoxin, penicillamine; theoretical increased risk of convulsions with mefloquine; reduces bioavailability of methotrexate; decreases plasma levels of praziquantel; increases incidence of mouth ulcers with proguanil
Contraindications: renal/hepatic insufficiency, severe blood or gastrointestinal disease, concomitant use of phenylbutazone, pregnancy (treatment, but regularly used in treatment of malaria; safe in prophylaxis), porphyria, epilepsy
TETRACYCLINE: oral (take ½ - 1 h before food); half life 9 h
Indications: symptomatic intestinal amoebiasis (not effective against liver abscess; may have limited activity for invasive intestinal disease); *Balantidium coli* enteritis; treatment of chloroquine resistant malaria
Side Effects: see Chapter 221
Contraindications: pregnancy, children ≤ 8 y
FURAZOLIDONE: nitrofuran
Indications: treatment of enteritis due to protozoans (including *Giardia intestinalis*) other than *Cryptosporidium*, *Cystoisospora belli*
Side Effects: tinnitus, hearing loss, vestibular symptoms
CRYSTAL VIOLET
Indications: trichomonal vaginitis (topical)
NATAMYCIN (PIMAFUCIN)
Indications: trichomonal vaginitis (topical)
NIMORAZOLE
Indications: trichomonal vaginitis
Contraindications: pregnancy, lactation
QUINACRINE
Indications: enteritis due to protozoans other than *Cryptosporidium*, *Cystoisospora belli*
Side Effects: yellow pigmentation of tissues, gastrointestinal disturbances, headache, uncommon allergic skin reaction, corneal edema, blood dyscrasias, toxic psychoses; increases toxicity of primaquine; ? disulfiram-like intolerance of alcohol
NITAZOXANIDE: not registered for use in Australia
Indications: cryptosporidiosis
Side Effects: most commonly, gastrointestinal
AMODIAQUINE
Indications: infections with *Leishmania*, *Plasmodium*
Side Effects: gastrointestinal disturbances, tiredness, vertigo, pigmentation of palate, nail beds and skin, uncommonly agranulocytosis, liver damage
HYDROXYCHLOROQUINE: oral (take with or after food)
Indications: infections with *Leishmania*; malarial prophylaxis
MEPACRINE
Indications: infections with *Leishmania*, *Plasmodium*, protozoans, tapeworms

PRIMAQUINE: tissue schizonticide; in WHO Model List of Essential Drugs for curative treatment of malaria; oral (take with or after food)

Indications: infections with *Leishmania,* prevention of delayed attacks of *Plasmodium ovale* and *Plasmodium vivax* by eradication of liver cycle; prevention of transmission of falciparum malaria

Side Effects: abdominal cramps and pain, epigastric distress, nausea and vomiting on an empty stomach common; hemolytic anaemia with large doses and in those with glucose-6-phosphate dehydrogenase deficiency, methemoglobinemia and cyanosis uncommon; cardiac arrhythmias, hypertension, anemia, leucopoenia, agranulocytosis, fever, rash rare; risk of toxicity increased by quinacrine; increases plasma levels and adverse effects of mefloquine

Contraindications: pregnancy, glucose-6-phosphate dehydrogenase deficiency (including breastfed infants; monitor also for hemolysis and jaundice in breastfed premature infants and those < 1 mo)

TAFENOQUINE: primaquine derivative

Indications: possibly more effective than primaquine in preventing relapse of *Plasmodium vivax* malaria

PROGUANIL (BIGUANIL, CHLOROGUANIDE): antifolate drug; in WHO Model List of Essential Drugs for malarial prophylaxis (usually in combination with chloroquine; increasing resistance); take with or after food (absorption enhanced)

Indications: infections with *Leishmania*; malarial prophylaxis where chloroquine cannot be administered

Side Effects: generally mild and self-limiting; mild gastric intolerance (vomiting, abdominal pain, diarrhoea with large doses only), aphthous ulcers (increased incidence with chloroquine), stomatitis common; scaling of skin, alopecia, vertigo uncommon; red cells and casts in urine with excessive amounts; marrow suppression, allergic reactions, convulsions, psychosis, disseminated intravascular coagulation, hepatitis, megaloblastic anemia rare; likely enhanced warfarin effect (frequent monitoring of prothrombin time essential); fluvoxamine decreases plasma levels and effect of active metabolite; absorption reduced by magnesium trisilicate; safety in pregnancy not established; safe in breastfeeding

PYRIMETHAMINE: selectively inhibits dihydrofolate reductase; half life 96 h; oral (take with or after food); in WHO Model List of Essential Drugs

Indications: infections with *Leishmania*, *Plasmodium*, *Toxoplasma gondii* (combined with another agent)

Side Effects: anorexia, vomiting, folinic acid reversible megaloblastic anemia, usually reversible leucopenia and other hematological toxicity with long term use, may be embryopathic; additional suppression of folate metabolism with cotrimoxazole, sulphonamides, trimethoprim and other folate antagonists (including cytostatic drugs) may result in serious pancytopenia and megaloblastic anemia, rarely aplasia; convulsions in children with CNS leukemia treated with methotrexate; dose adjustment not required in renal failure or in dialysis but monitor for myelosuppression; safety in pregnancy not established; safe in breastfeeding

PYRIMETHAMINE-DAPSONE: interferes with folate metabolism; dapsone half life 21 h

Indications: previously used for malaria prophylaxis

Side Effects: agranulocytosis, cyanosis, allergic dermatitis, gastrointestinal disorders, acute hemolysis in individuals with glucose-6-phosphate dehydrogenase deficiency; safety in pregnancy not established

Contraindications: avoid if breastfeeding G6PD deficient infants; monitor for hemolysis and jaundice if breastfeeding premature infant or < 1 mo old; avoid high doses if breastfeeding any infant (may interfere with folic acid metabolism)

PYRIMETHAMINE-SULPHADOXINE: interferes with folate metabolism; in WHO Model List of Essential Drugs as complementary drug for curative treatment of malaria when drugs in main list are known to be ineffective or inappropriate for a given individual; half life sulphadoxine 200 h; take with or after food

Indications: treatment of chloroquine resistant *Plasmodium falciparum* malaria (resistance increasing); maintenance therapy for *Isospora belli* enteritis

Side Effects: erythema multiforme, orogenital lesions, pharyngitis, pruritis, rash, agranulocytosis, exfoliative dermatitis, serum reaction type reaction, urticaria, gastrointestinal disturbances, induction of folate deficiency; Stevens-Johnson syndrome (can be fatal), toxic epidermal necrolysis rare; much more common when taken in combination with chloroquine

Contraindications: pregnancy; neonatal period; avoid if breastfeeding premature infant or infant < 1 mo or with G6PD deficiency

PYRIMETHAMINE-SULPHALENE

Indications: malaria prophylaxis

QUININE: rapidly acting blood schizonticide; in WHO Model List of Essential Drugs for curative treatment of malaria; oral (take with or after food) and parenteral; half life 10 h

Indications: babesiosis; infections with *Leishmania*; chloroquine-resistant severe falciparum malaria

Side Effects: tinnitus and auditory ototoxicity, headache, gastrointestinal disturbances (nausea, abdominal pain), photosensitivity, visual disturbance and impairment, urticaria, rashes, generalised cutaneous erythema and pruritis, confusion (idiosyncrasy or excessive dosage), fever, dyspnea, hypoglycemia, thrombocytopenia common; severe intravascular hemolysis in patients with G6PD deficiency; allergy, hyperinsulinemia, acute renal failure, angioedema rare; toxicity increased by pyrimethamine; must never be given by i.v. bolus injection; dose interval adjustment required in renal failure and in dialysis;

unpredictably increases effect of oral anticoagulants; increased risk of QT prolongation with all drugs prolonging QT interval; may increase plasma levels of mefloquine, with theoretical increased risk of convulsions
Contraindications: pregnancy, hemolysis, tinnitus, optic neuritis; avoid if breastfeeding G6PD infant; monitor breastfed premature infant or infant < 1 mo for haemolysis and jaundice
QUINIDINE GLUCONATE
Indications: chloroquine-resistant severe malaria if quinine dihydrochloride unavailable
Side Effects: hyperinsulinemia, hypoglycemia, cardiotoxicity (serious ventricular arrhythmia); never give by i.v. bolus injection
MEFLOQUINE: blood schizonticide; in WHO Model List of Essential Drugs in main list for prophylaxis of malaria and as complementary drug for curative treatment of malaria when drugs in main list are known to be ineffective or inappropriate for a given individual; oral (take with or after food); half life 21 d
Indications: curative treatment of malaria due to chloroquine resistant *Plasmodium falciparum*; malarial prophylaxis in areas with chloroquine resistant *Plasmodium falciparum*; use at present highly restricted in order to minimise development of resistance (increasing in Thailand, Cambodia and Myanmar)
Side Effects: nausea in 4%, depression, lethargy, bad dreams in 2%, vertigo in 2%, vomiting, diarrhoea, fever in 1%, tachycardia in 0.7%, euphoria in 0.7%; dyspepsia, dizziness, loss of balance, headache, insomnia, mental clouding, difficulty in performing skilled tasks also common; myalgia, rash, paresthesia, visual disturbances, elevated transaminases, seizure, chest pain, edema uncommon; severe neuropsychiatric adverse events in 0.01-0.5%; erythema multiforme, blood dyscrasias, hyperpyrexia rare; increased risk of convulsions with chloroquine, quinine, quinidine; ECG abnormalities reported with β-blockers, quinidine; increased risk of bradycardia with beta-blockers, calcium channel blockers, digoxin; significant cardiotoxic reactions in patients treated with halofantrine after taking mefloquine for prophylaxis; primaquine and quinine increase plasma levels; safety in pregnancy not established; caution in breastfeeding (monitor infant for adverse effects); dose modification not required in renal failure or in dialysis
Contraindications: children < 8 kg, patients with known hypersensitivity to mefloquine or related compounds (quinine, quinidine), neuropsychiatric disorders, epilepsy or cardiac conduction abnormalities or on drugs altering cardiac conduction
ITRACYCLINE
Indications: curative treatment of malaria
DOXYCYCLINE: blood schizonticide; in WHO Model List of Essential Drugs
Indications: treatment of chloroquine resistant malaria; malarial prophylaxis where chloroquine cannot be administered or in high risk individuals in areas with chloroquine resistant *Plasmodium falciparum*
Side Effects: see Chapter 21
Contraindications: pregnancy, children ≤ 8 y
QUINGHAOM (ARTEMETHER, ARTEMISATE, ARTEMISININ): artemether in WHO Model List of Essential Drugs
Indications: treatment of chloroquine resistant malaria
Contraindications: pregnancy (first trimester), avoid in breastfeeding (insufficient data)
ARTEMETHER + LUMEFANTRINE: oral; bioavailability increased when taken with fatty food
Indications: treatment of acute uncomplicated malaria due to *Plasmodium falciparum* in individuals ≥ 12 y and 35 kg; no significant effects on cardiac conduction and no interaction with mefloquine; oral (take with or after food)
Side Effects: headache, dizziness, sleep disorders, palpitations, anorexia, abdominal pain, nausea, vomiting, dyspepsia, diarrhoea, myalgias, arthralgia, fever, asthenia, fatigue, rigours, pruritis common
Contraindications: pregnancy (first trimester), avoid in breastfeeding (insufficietn data)
ARTESUNATE: artemisin derivative
Indications: mefloquine resistant malaria, severe malaria (i.v.)
Side Effects: safety in pregnancy and breastfeeding not known (do not withhold in severe malaria)
HALOFANTRINE
Indications: treatment of chloroquine resistant malaria; postexposure malarial prophylaxis for high risk individuals in areas with chloroquine resistant *Plasmodium falciparum*
Side Effects: potentially fatal cardiotoxicity (potentiated by mefloquine and macrolides)
Contraindications: pregnancy
CORTICOSTEROIDS
Indications: hyperreactive malarial splenomegaly; *Toxoplasma* anterior uveitis and retinochoroiditis; severe visceral larva migrans
SODIUM STIBOGLUCONATE: solution must be protected from light
Indications: leishmaniasis; schistosomal enteritis, hepatitis, hepatic granuloma and urinary infection
Side Effects: arthralgia, blood dyscrasias, cardiotoxicity (ECG change, T wave depression, prolongation of QT interval, fusion of ST segment and T waves), hepatitis, myalgia, pneumonitis, pancreatitis (especially renal transplant recipients)

Meglumine Antimonate: in WHO Model List of Essential Drugs
Indications: leishmaniasis (92% cure rate in cutaneous, 66% in visceral), schistosomiasis
Side Effects: chemical pancreatitis in 30%, cardiotoxicity in 14%
Pentamidine Isethionate: in WHO Model List of Essential Drugs as main list drug to improve compliance
Indications: babesiosis; leishmaniasis (95% cure rate in cutaneous); treatment and prophylaxis of hemolymphatic trypanosomiasis due to *Tyrpanosoma brucei gambiense*
Side Effects: i.v.: immediate hypotension, nausea and vomiting; later, local pain at injection site, abscess formation, neutropenia (frequent in AIDS), thrombocytopenia, rash (rare), nephrotoxicity (mild azotemia to severe tubular necrosis), hepatitis with abnormal liver function tests, hypoglycemia and hyperglycemia, cardiotoxicity in 23% of patients treated for antimony-resistant kala azar, hypomagnesia, hypokalemia, acute pancreatitis, ventricular arrhythmias; severe hypocalcemia with foscarnet; possible potentiation of toxic effects on rapidly growing cells (bone marrow, spermatogonia, germinal layers of skin and gastrointestinal mucosa) with ganciclovir; possible potentiation of nephrotoxicity (including acute renal failure) with amphotericin, cidofovir, foscarnet, other nephrotoxic agents; diabetes in 20% of patients treated for 3 weeks; increased risk of QT prolongation with all drugs capable of prolonging QT interval; dose adjustment required in renal failure, not in dialysis (except continuous venovenous or arteriovenous hemodialysis); aerosolised: bronchospasm, acute pancreatitis, mild hypoglycemia, increased risk of spontaneous pneumothorax; safety in pregnancy not established
Contraindications: avoid in breastfeeding (insufficietn data)
Allopurinol
Indications: isolated skin lesions due to *Leishmania braziliensis, Leishmania mexicana*; visceral leishmaniasis
Side Effects: skin rash, mild fever, dyspepsia, nausea, vomiting, colic, diarrhoea, drowsiness, headache, peripheral neuritis, liver enlargement
Ketoconazole
Indications: isolated skin lesions due to *Leishmania braziliensis*, *Leishmania mexicana*
Side Effects: see Chapter 22
Interleukin 2
Indications: isolated skin lesions due to *Leishmania braziliensis*, *Leishmania mexicana*
Methylbenzethonium
Indications: localised skin lesions due to *Leishmania tropica*
Gamma Interferon
Indications: visceral leishmaniasis
Miltefosine: oral
Indications: visceral leishmaniasis
Pyrimethamine-Sulphadiazine
Indications: *Toxoplasma* brain and epidural abscess, encephalitis (80-90% effective), meningitis, retinochoroditis, infections in pregnancy
Side Effects: seen in 30-45% of patients; severe skin rash, leucopoenia, thrombocytopenia, elevated levels of serum transaminases, bone marrow toxicity, pancytopenia, megaloblastic anemia
Sulphonamides
Indications: cerebral toxoplasmosis in AIDS
Side Effects: see Chapter 21
Azithromycin: macrolide
Indications: treatment of cerebral toxoplasmosis in AIDS
Side Effects: see Chapter 21
Cotrimoxazole
Indications: enteritis due to *Isospora belli*; *Toxoplasma gondii*; toxoplasmosis (including anterior uveitis, brain and epidural abscess, hydrocephalus, hepatitis and hepatic granuloma, pancreatitis, prophylaxis in AIDS); in WHO Model List of Essential Drugs
Side Effects: see Chapter 21
Spiramycin: macrolide
Indications: enteritis due to *Cryptosporidium*; toxoplasmosis (including meningitis, pancreatitis)
Side Effects: see Chapter 21
Erythromycin: macrolide
Indications: enteritis due to *Cryptosporidium*
Side Effects: see Chapter 21
Roxithromycin: macrolide
Indications: enteritis due to *Isospora belli*
Side Effects: see Chapter 21

5-Fluorouracil

Indications: *Toxoplasma* encephalitis

Side Effects: diarrhoea, nausea, vomiting, alopecia, dermatitis, pigmentation, changes in nails, ataxia, fever, leucopenia, thrombocytopenia, chest pain, tachycardia, breathlessness, arrhythmia, ECG changes

Clindamycin

Indications: babesiosis; *Toxoplasma* encephalitis and retinochoroiditis

Side Effects: see Chapter 21

Dapsone

Indications: toxoplasmosis prophylaxis in AIDS

Side Effects: see Chapter 21

Atovaquone: take with or after food (absorption enhanced); absorption reduced in patients with severe diarrhoea; plasma levels significantly reduced by metoclopramide, rifampicin

Indications: prophylaxis and treatment of *Plasmodium falciparum* malaria (in combination with proguanil)

Side Effects: occasional rash, fever, elevated liver function tests, abdominal pain, vomiting, nausea, diarrhoea, anorexia, headache, dizziness, myalgia; probably safe in regnancy

Contraindications: avoid in breastfeeding (insufficient data)

Eflornithine: in WHO Model List of Essential Drugs as complementary drug for use in rare disorders or in exceptional circumstances

Indications: African trypanosomiasis

Calcium Folinate

Indications: prevention of anemia in treatment of toxoplasmosis with pyrimethamine + sulphonamides

Bicanthone

Indications: *Schistosoma haematobium* infections

Hycanthone

Indications: schistosomiasis

Metrifonate

Indications: schistosomiasis haematobium (cure rate 18% alone, 25% combined with niridazole)

Side Effects: nausea, vomiting, headache, possible hemolysis in subjects with glucose-6-phosphate dehydrogenase deficiency

Contraindications: pregnancy

Oxamniquine: in WHO Model List of Essential Drugs; relatively expensive

Indications: schistosomiasis due to *Schistosoma mansoni*

Side Effects: toxicity is insignificant

Niridazole

Indications: dracunculiasis; schistosomiasis due to *Schistosoma haematobium, Schistosoma japonicum*

Praziquantel: in WHO Model List of Essential Drugs; oral (take with or after food); relatively expensive

Indications: biliary cirrhosis due to flukes; cholangitis and cholecystitis due to helminths; clonorchiasis; cysticercosis; enteritis due to *Diphyllobothrium*, flukes, *Hymenolepis*, *Taenia*; fascioliasis; paragonimiasis; schistosomiasis (including Katayama syndrome; all species; cure rate 47%); taeniasis (including neurocysticercosis)

Side Effects: drowsiness in 70%, mild abdominal pain in 43%, urge to defecate in 40%, diarrhoea in 30%, fever in 27%, nausea in 15-40%, vomiting in 15-17%, vertigo in 12-40%, hepatomegaly in 4.5%, pruritis in 3%, headache in 1.5-57%, rash in 1.5%, hypotension in 1.5%; dizziness, malaise, colic, elevated transaminases also common; focal seizures, motor weakness, skin reactions, eosinophilia, fever, anorexia, papilledema rare; increased in presence of liver disease; alcohol increases risk of CNS toxicity; carbamazepine, phenytoin, chloroquine, dexamethasone decrease plasma levels; cimetidine increases plasma levels; increases risk of albendazole adverse effects; probably safe in pregnancy; safe in breastfeeding; dose modification not required in renal failure or in dialysis

Trichlorofon

Indications: urinary schistosomiasis

Melarsopol: in WHO Model List of Essential Drugs as main list drug to improve compliance

Indications: cerebral trypanosomiasis and hemorrhagic fever due to *Trypanosoma brucei rhodesiense*

Side Effects: very toxic; must only be given under medical supervision

Suramin Sodium: in WHO Model List of Essential Drugs as main list drug for African trypanosomiasis and complementary antifilarial drug when drugs in main list are known to be ineffective or inappropriate for given individual and for which specific expertise, diagnostic precision, individualisation of dosage or special equipment is required for proper use and for which adverse effects diminish benefit/risk ratio

Indications: African trypanosomiasis (special cases, including hemorrhagic fever); onchocerciasis (if ocular microfilariae present after diethylcarbamazine and nodulectomy)

Side Effects: nephrotoxic; must be given under medical supervision; routine urine tests needed to detect albumin losses which, if present, contraindicate further suramin treatment

NITROFURAZONE

Indications: CSF infection with *Trypanosoma brucei*

DIFLUOROMETHYLORNITHINE HYDROCHLORIDE MONOHYDRATE

Indications: CSF infection with *Trypanosoma brucei*

LAMPIT

Indications: American trypanosomiasis

BENZIMIDAZOLE: in WHO Model List of Essential Drugs as drug for which adverse effects diminish benefit/risk ratio

Indications: American trypanosomiasis

NIFURTIMOX: in WHO Model List of Essential Drugs as drug for which specific expertise, diagnostic precision, or special equipment is required for use and which has limited indications or narrow spectrum of activity

Indications: American trypanosomiasis

DIETHYLCARBAMAZINE: in WHO Model List of Essential Drugs; oral (take with or after food)

Indications: antifilarial; visceral larva migrans

Side Effects: nausea, dizziness; allergic reaction with fever, rashes and malaise may occur after first dose; may provoke encephalopathy in heavy infection with *Onchocerca volvulus*; Mazzotti reaction (intractable fever, pruritis, adenitis, iritis, hypotension) may occur (manage with antipyretics, antihistamines, analgesics); safety in pregnancy not established

Contraindications: renal disease

FLUBENDAZOLE

Indications: filariasis; infections with *Ascaris* (single dose cure rate 94%), hookworm (single dose cure rate 75%), *Trichuris* (cure rate 32%); onchocerciasis

Side Effects: severe reaction at site of injection, 'flu-like' reactions after treatment for 3-5 w

IVERMECTIN: in WHO Model List of Essential Drugs; oral (best taken with food)

Indications: antifilarial; antihelminthic (single dose cure rate 100% for *Ascaris lumbricoides* and *Strongyloides stercoralis*, 50% for *Trichuris trichuria*, 20% for hookworm); onchocerciasis; Norwegian scabies; cutaneous larva migrans; head lice; gnathostomiasis

Side Effects: transient sensitivity reactions responding to analgesics and antihistamines in filariasis; more likely in treatment for onchocerciasis than for strongyloidiasis; nausea, diarrhoea, dizziness, pruritis common; constipation, vomiting, tremor, rash, fatigue uncommon; headache, postural hypertension, tachycardia, myalgia, facial and peripheral edema, eye inflammation rare; safety in pegnancy not established; safe in breastfeeding

Contraindications: children < 15 kg

SODIUM ANTIMONY DIMERCAPTOSUCCINATE

Indications: fascioliasis; paragonimiasis; taeniasis

BITHIONOL

Indications: enteritis due to *Nanophyetus salmincola*; fascioliasis (including hepatitis and hepatic granuloma); paragonimiasis

HEXYLRESORCINOL

Indications: enteritis due to *Fasciolopsis buski*

TETRACHLOROETHYLENE

Indications: enteritis due to flukes

PIPERAZINE CITRATE

Indications: ascariasis (intestinal obstruction); enterobiasis

Side Effects: nausea, vomiting, diarrhoea, lack of muscular coordination, abdominal pain; rarely, dizziness, allergy, rash

Contraindications: epilepsy, renal failure, liver disease; caution in impaired renal function, psychiatric states, neurological disease

THIABENDAZOLE: benzimidazole; deleted from WHO Model List of Essential Drugs because of general toxicity; take with or after food (twice daily)

Indications: cutaneous larva migrans; dracunculiasis; parasitic hepatic granuloma; infections with helminths including *Anisakis*, *Echinococcus*, *Phocanema*, *Pseudoterranova, Strongyloides* (including enteritis, meningitis, diffuse interstitial pneumonia; cure rate 75-95%), *Trichostrongylus* and *Trichinella*; larval pneumonitis; spirometrosis; visceral larva migrans; toxocariasis

Side Effects: diarrhoea and colic common in heavily infected children; nausea, vomiting, headache uncommon; dizziness, pruritis, paresthesia, cholestatic jaundice, elevated transaminaes, allergic reactions, Stevens-Johnson syndrome, proteinuria, neutropenia, alopecia, thrombocytopenia rare; single case report of tinnitus; safety in pregnancy not established; may increase theophylline plasma levels; dose modification not required in renal failure or in dialysis

Contraindications: first trimester; children < 6 mo; avoid if breastfeeding (insufficient data)

ALBENDAZOLE: benzimidazole; for intraluminal infections, take on an empty stomach, otherwise with or after food (absorption enhanced); in WHO Model List of Essential Drugs; expensive

Indications: echinococcosis (in conjunction with surgery); infections with *Ancyclostoma* (single dose cure rate 96%), *Ascaris* (single dose cure rate 96%), *Enterobius vermicularis*, *Necator* (single dose cure rate 90%), *Strongyloides stercoralis* (cure rate 48%), *Trichuris* (cure rate 76%); neurocysticercosis; prophylaxis in children in communities with heavy intestinal helminth exposure; trichinellosis (including myocarditis and pericarditis); filariasis; capillariasis; trichinosis; toxocariasis; cutaneous larva migrans; giardiasis

Side Effects: as for **THIABENDAZOLE**; increased by praziquantel; dose modification not required in renal failure; dose after intermittent haemodialysis

Contraindications: pregnancy, children < 6 mo

LEVAMISOLE: in WHO Model List of Essential Drugs as drug with limited indications or narrow spectrum of activity

Indications: halzoun; infections with *Ascaris*, *Enterobius*, hookworms, *Strongyloides*, *Trichuris;* lagochilascariasis

MEBENDAZOLE: benzimidazole; in WHO Model List of Essential Drugs; broad spectrum; for intestinal worms, take on an empty stomach; for systemic infections, take with or after food; possible increase in plasma levels due to inhibition of metabolism with cimetidine

Indications: eosinophilic meningitis; larval pneumonitis; worms other than tapeworms (including *Ascaris* (cure rate > 90%), *Enterobius,* hookworm (cure rate 81-95%), *Strongyloides stercoralis*, *Taenia solium, Trichinella, Trichuris* (cure rate 90%))

Side Effects: as for **THIABENDAZOLE**; carbamazepine, phenytoin decrease plasma levels; cimetidine increases plasma levels; safety in pregnancy not established; safe in breastfeeding; dose modification not required in renal failure or in dialysis

Contraindications: first trimester, children < 6 mo, patients who have experienced allergic reactions to it

LOPERAMIDE

Indications: treatment of diarrhoea preparatory to treatment with mebendazole in *Trichuris trichuria* enteritis

Side Effects: usually minor and self-limiting; constipation, CNS depression, gastrointestinal irritation with overdosage

DEXAMETHASONE

Indications: eosinophilic meningoencephalitis; neurocysticercosis

OXANTEL PAMOATE

Indications: infections with *Ascaris* (cure rate 21%), hookworm (cure rate 38%), *Trichuris* (single dose cure rate > 70%)

PYRANTEL (EMBONATE AND PAMOATE): in WHO Model List of Essential Drugs; oral (take with or after food)

Indications: cutaneous larva migrans; eosinophilic meningitis; infections with *Ancyclostoma duodenale* (single dose cure rate 97-98%), *Ascaris* (single dose cure rate > 90%), *Enterobius*, *Necator americanus* (single dose cure rate 74-75%); larval pneumonitis; prophylaxis in children in communities with heavy intestinal helminth exposure

Side Effects: nausea, vomiting, abdominal discomfort/cramps, diarrhoea, headache common; dizziness, drowsiness, anorexia, tenesmus, rash, insomnia, fatigue rare; occasional minor abnormalities of liver function (elevated transaminases); safety in pregnancy not established; safe in breastfeeding and in children < 6 mo

PREDNISONE

Indications: cutaneous larva migrans; neurocysticercosis; spirometrosis

METHYLPREDNISOLONE ACETATE

Indications: intraocular *Taenia solium* cysts (periocular)

CONBENDAZOLE

Indications: intestinal roundworm infections

ETHYL CHLORIDE

Indications: cutaneous larva migrans and spirometrosis (topical)

FEBANTEL

Indications: intestinal roundworm infections

PYRVINIUM EMBONATE AND PAMOATE

Indications: enteritis and vaginitis due to *Enterobius vermicularis*

NICLOSAMIDE: take with or after food; in WHO Model List of Essential Drugs

Indications: infections with tapeworms including *Diphyllobothrium*, *Hymenolepis nana, Nanophyetus salmincola, Taenia*, tongue worms

Side Effects: rarely, abdominal pain, nausea, vomiting; probably safe in pregnancy

BENZYL BENZOATE: in WHO Model List of Essential Drugs

Indications: pediculosis, scabies; all household members should be treated

Side Effects: occasional skin sensitisation; safe in children; safety in pregnancy not established; caution in breastfeeding (prefer permethrin)

CROTAMITON
Indications: scabies in patient < 2 mo
Side Effects: safety in pregnancy not established
LINDANE (GAMMA BENZENE HEXACHLORIDE)
Indications: grain itch, pediculosis pubis, scabies
Side Effects: eczematous eruptions due to sensitisation; seizures; aplastic anaemia; safety in pregnancy not established
Contraindications: lactation, children < 2 y.o.
MALDISON
Indications: pediculosis and phthiriasis
Side Effects: safety in pregnancy not established
Contraindications: avoid if breastfeeding (insufficient data)
PYRETHRIN
Indications: fogging of sources of infestations
Contraindications: safety in pregnancy and lactation not established
PYRETHRINS + PIPERONYL BUTOXIDE
Indications: pediculosis and phthirasis; safe in children; safety in pregnancy not established
PERMETHRIN: in WHO Model List of Essential Drugs
Indications: infestations
Side Effects: safety in pregnancy not established; safe in breastfeeding
SULPHUR
Indications: scabies in patient < 2 mo
AMITRYPTYLINE
Indications: ciguatera fish poisoning
Side Effects: the wide range of adverse reactions, affecting all organ systems, attributable to amitriptyline are unlikely to be seen with the suggested regimen (except, perhaps, for drowsiness and anticholinergic effects)
ANTITOXIN
Indications: tick paralysis
DIETARY RESTRICTION
Indications: acute diarrhoea and/or vomiting
DRAINAGE
Indications: amoebic hepatic abscess if no response to chemotherapy after 5 d, abscess > 10 cm or suspected impending rupture
ETHANOL
Indications: echinococcosis (injected into cyst and reaspirated)
EXCHANGE TRANSFUSION
Indications: babesiosis; malaria due to chloroquine resistant *Plasmodium falciparum*
EXCISION
Indications: thyroiditis
INTRAVENOUS FLUIDS
Indications: dehydration in acute diarrhoea and/or vomiting
REHYDRATION
Indications: dehydration in acute diarrhoea and/or vomiting
SURGERY
Indications: cerebral spirometrosis; echinococcosis; hydrocephalus due to *Toxoplasma gondii*; neurocysticercosis with ventricular involvement or raised intracranial pressure; parasitic eye infections; raised intracranial pressure due to hydatid cyst; trichinellosis

Part 4: Laboratory Procedures

Chapter 24

Collection, Handling and Processing of Specimens

The correct specimen (as specified in earlier chapters) must be collected.

Expectorated **sputum** is an unreliable source of specimens; the frequency of confusing Gram negative bacteria has been reported at 31%. Sterile saline washing of expectorates has been found tedious and hazardous. To be of value, sputum must have been derived from deep in the respiratory tract. It should be screened for evidence of contamination with oral secretions. Specimens with < 10 squamous epithelial cells/100X field may be of satisfactory quality, especially if containing > 25 polymorphonuclears/100X field. Gram stain should always be done; 97% of *Streptococcus pneumoniae* and *Haemophilus influenzae* infections are detected by Gram stain-directed culture versus 51% by routine culture; overall specificity is 90% but sensitivity is 60-85%. *Streptococcus pneumoniae* isolation may improve if plating occurs within 1 h of collection. > 10 bacteria of the same kind per 1000X field should be reported and a definite identification in cultures attempted. A combination of coagglutination and semiquantitative, microscopy-directed culture of homogenised sputum is optimal. A culture of > 100,000-1M/mL of bacteria preliminarily identified in the Gram should be regarded as significant. Pneumococcal antigen detection, direct fluorescent antigen and culture for *Legionella,* DNA probe for *Mycoplasma pneumoniae*, smear for *Mycobacterium tuberculosis*, monoclonal antibody fluorescence for *Pneumocystis jiroveci* and viral antigen detection tests can also be performed on sputum.

If an adequate specimen of sputum cannot be obtained, if there is no clear diagnosis from expectorated sputum, or if there is poor response to antibiotics chosen on the basis of an expectorated sample, bronchoalveolar lavage is the safest, most reliable method of obtaining authentic specimens. Gram stain and culture should be performed, with > 10,000-100,000 bacteria/mL of fluid being regarded as significant. Pneumococcal antigen detection, direct fluorescent antigen and culture for *Legionella*, DNA probe and culture for *Mycoplasma pneumoniae*, monoclonal antibody fluorescence for *Pneumocystis jiroveci*, smear and culture for *Mycobacterium tuberculosis* and virus isolation can also be performed. For paediatric patients, a specimen may be collected by a respiratory therapist via suction. Gram stain and culture of a bronchoscopy protected specimen brush (with 10,000 bacteria/mL significant) and viral antigen detection in cells may be useful, as may Gram stain, viral culture, pneumococcal antigen detection on pleural fluid. Urine may be used for *Legionella* antigen detection.

Urinary tract specimens for anaerobes should be suprapubic percutaneous bladder aspirates. In other cases, contamination with urethral and perineal flora should be avoided. Mid-stream clean catch specimens are suitable for most purposes. Catheter specimens do not distinguish between colonisation and infection and procedure may introduce urethral flora into bladder. Suprapubic aspiration is the best way to obtain an uncontaminated specimen when this is not possible by normal means. Urine from urinary tract diversion specimens has a rich mixed aerobic and anaerobic flora (uterosigmoidostomy > ileal conduit > colon loop). Culture of such specimens is irrelevant and antimicrobial treatment useless. Ascorbate may lessen development of malignancy. Foley catheters are not acceptable for culture, since growth represents distal urethral flora.

Urine specimens should be refrigerated immediately upon receipt in the laboratory unless they are processed at once. Most uropathogens grow well in urine held at room temperature. However, bacterial counts should remain stable for at least 24 h at 4°C. The use of a dip slide at the time of collection to establish the true count is good practice. As the time a specimen is left unrefrigerated increases, so does the percentage of mixed cultures. Less than 5% of urines which are properly collected and transported contain multiple organisms. Exceptions to this rule are urine specimens from patients with neurogenic bladders or chronic indwelling catheters, in which polymicrobic bacteriuria may be detected in 30-80% of cultures. The Becton-Dickinson Urine Culture Tube is useful where there is considerable delay between collection and processing (up to 24 h), though a possibly better system is provided by using a lyophilised preservative containing boric acid, sorbitol and sodium formate; this provides 94% agreement with fresh specimens in microscopy and 96% agreement in culture after 48 h.

Of the many rapid methods for detecting bacteriuria available, acridine orange staining is the most sensitive (98% at 10,000 cfu/mL, 99% at 100,000 cfu/mL), requires only 2 minutes and costs only 50 cents per test. However, it does require fluorescent equipment. Gram stain for the presence of bacteria in an uncentrifuged urine specimen has a sensitivity of 80% and specificity of 90%. The urine dipstick leucocyte esterase and nitrite tests have sensitivity of 79-88% and specificity of 80-96%. These results are superior to microscopic analysis for pyuria. Chemstrip LN and Bac-T-Screen both

detect bacteriuria and pyuria. Both take 2 minutes per test and have 93-94% sensitivity at detecting pyuria (lower in leucopenic patients). The Bac-T-Screen is more sensitive at detecting bacteriuria (93% at 10,000 cfu/mL and 97% at 100,000 cfu/mL versus 79% and 92%) but costs nearly 3 times as much per test. The Lumac system has the highest sensitivity (98%) and predictive value of negative (99.5%), takes 35 minutes and is 50% more expensive again. The most effective method appears to be screening of urines at the point of collection with Boehringer Mannheim Combur-9 dipsticks, eliminating all urines which do not show any abnormality; this gives a virtually 100% correlation with full laboratory testing. The IRIS automated urine microscopy detects more than twice as many abnormalities as are found by manual microscopy, but it remains to be proved that the significance of this is such as to justify its cost. The presence of leucocytes and/or hematuria and/or bacteria on microscopy suggests, but does not prove, urinary tract infection. Many patients with increased numbers of white cells in the urine do not have urinary tract infection. The most common cause is probably vaginal contamination, but inflammatory processes anywhere in the body may result in the presence of increased numbers of leucocytes in the urine. Again, many patients with urinary tract infection do not have increased numbers of white cells in the urine. Dysmorphic red cells are seen in patients with glomerular disease. Such patients should be investigated with renal function assessments and possibly a renal biopsy.

If standard culture methods are used, results can be speeded up by realising that 85% of urines with 100,000 organisms/mL will, after 4-6 h incubation, produce recognisable colonies which can be presumptively identified by a combination of colonial morphology and spot tests with an accuracy of > 90%. Specimens from patients with urinary tract infection usually produce counts of > 100,000. Lower counts are related to contamination from external urethra and vagina. Specimens from patients without infection will generally cluster < 1000. At the 10,000-100,000 level, there is a 5% chance of infection, and cultures should be repeated. Two specimens yielding a titre of 100,000 or more make the probability of infection about 95%. False positives are found mainly in women and are related to contamination. False negatives are related to patients taking antimicrobials, diuresis or rare tuberculous or anaerobic infections. Enterococci, staphylococci and diphtheroids do not grow well in urine and will sometimes show up as borderline cultures (10,000-100,000). A titre of 10,000 of Gram positive organisms is cause for suspicion warranting a repeat culture. *Haemophilus* infections constitute 0.3% of urine cultures; this does not warrant routine screening but, in the case of abnormalities of the urinary tract with recurrent infections, especially in young girls, and when results suggest infection in the presence of negative cultures, the possibility of *Haemophilus* infection should be considered and appropriate media employed. Cultures for other fastidious organisms (*Mycobacterium, Ureaplasma urealyticum, Gardnerella vaginalis*, anaerobes) may also be warranted. The adoption of a criterion of infection of a colony count of 10,000/mL in urines with 10,000 leucocytes/mL of uncentrifuged urine and of 100,000/mL in those with < 10,000/mL gives a sensitivity and specificity of 99%.

Blood cultures: Isolates from blood cultures should always be fully identified and no isolate should be discarded as a contaminant without proper investigation. A single draw of 35-42 mL maximises sensitivity and minimises risk of contamination.

The use of a biphasic bottle frequently allows earlier isolation, in most cases enabling colonies to be picked and used in identification and susceptibility tests as soon as growth is evident. Caution should, however, be used in interpreting rapid staphylococcal fibrinogen/protein A tests and oxidase tests on colonies taken from the slopes of these bottles; they frequently give misleading results. This system also allows greater recovery of *Streptococcus pneumoniae* and simplifies the subculture process, resulting in decreased labour, contamination and cost. *Pseudomonas,* coagulase negative *Staphylococcus, Staphylococcus aureus, Bacillus, Escherichia coli, Klebsiella, Serratia, Acinetobacter, Alcaligenes, Neisseria* and *Candida* show diminished growth in unvented vacuum-exhausted bottles, while significantly more isolates of *Corynebacterium, Haemophilus, Flavobacterium, Moraxella, Bacteroides* and *Peptostreptococcus* are recovered from unvented bottles. Therefore, one type only should never be used. Routine subculturing of biphasic bottles is unnecessary, but unvented bottles should routinely be subcultured at 6-17 h and again at 48 h. If a biphasic bottle is not used, the vented bottle should be treated similarly. In this case, also, agitation of the vented bottle significantly decreases the detection time and increases the number of positive blood cultures detected. Contamination rates and costs with these systems are about equal to the biphasic. Repeat subculture of known positive blood cultures is costly and ineffective in detecting polymicrobial bacteremias. Isolation rates can be significantly increased by use of lysis-centrifugation, eg, DuPont Isolator. This gives > 10% higher isolation rates than conventional 2 bottle systems (especially *Staphylococcus aureus*, fungi and mycobacteria, although the additional of oleic acid to conventional systems increases the yield of the latter to an equivalent extent), but recovery of *Streptococcus pneumoniae* is less good than with conventional systems and the contamination rate is 12% higher. The method involves direct plating of the system, eliminating subculture. This method is also useful for viral isolation and should always be used in investigating fungemia. With patients receiving i.v. lipids, media containing 2.5% olive oil should be used. The method's main advantage is in decreasing detection time. Isolation rates also depend on the volume of blood cultured, average yields from 30 mL of blood being 61% greater than that from 10 mL of blood.

The Bactec automated system provides similar isolation rates to conventional methods (except for *Streptococcus pneumoniae*, also, *Coccidioides immitis* produces visible growth but a negative growth index) and is cost effective for volumes in excess of about 6000 specimens per year. Cost per bottle is only about 40% of that for Isolator and biphasic

systems, while labour involved is about equal to the biphasic. The radiometric system can also be used for rapid identification of mycobacteria.

Antimicrobials present in blood can frequently be removed by use of Bactec 16B medium (which does not always work for ticarcillin or moxalactam) or Marion's antimicrobial removal device (which may not work for moxalactam, cefotaxime or cefoperazone). However, studies have not convincingly shown that this translates into a higher yield of positives. On the other hand, the membrane filtration technique of Sullivan, Sutter and Finegold yields twice as many positives as the best conventional system from patients on antimicrobial therapy.

Gram staining should be the first step in investigating any positive blood culture. Gram positive cocci will almost always be staphylococci, streptococci or anaerobic cocci. 99% of staphylococci and streptococci can be correctly identified by microscopy. *Neisseria, Haemophilus, Bacteroides* and Gram positive bacilli can also usually be identified from microscopy. If diphtheroids are seen, it may be worth while doing a hanging drop preparation to look for the distinctive tumbling motility of *Listeria monocytogenes*.

It is frequently possible to obtain a quick identification of *Escherichia coli* by spinning down a portion of the culture fluid and performing an indole test on the supernate. Direct inoculation of MICROID or API20E from the culture fluid is also frequently possible, while the AMS (Vitek) will often give a direct identification in 3-8 h and direct susceptibility in 5-8 h. Blood for viral culture (*human cytomegalovirus* and *simplexvirus* virus routinely isolated; arboviruses, arenaviruses, *Epstein-Barr virus*, *HIV-1* and enterovirus in newborns not routinely isolated) should be collected during the acute phase of the infection and not refrigerated.

Blood cultures should also be obtained when a **CSF** specimen is taken. If only one tube of CSF is collected, it should be submitted to microbiology first; otherwise, the second tube collected is usually used. *Coxsackievirus*, echovirus, enterovirus and *mumps virus* are routinely cultured from CSF. Arboviruses, *simplexvirus* virus, *lymphocytic choriomeningitis virus* and *rabies virus* may also be cultured, but this is not routinely done.

Contamination and drying of **routine smears and cultures for bacteria (including mycobacteria) and fungi** must be avoided.

Wound swabs should be taken from the advancing margin of the lesion. For abscesses, tissue or fluid is always superior to a swab. If swabs must be used, 2 should be collected: 1 for culture and 1 for Gram stain. Agents are usually not recovered from animal bite wounds < 12 h old. The yield of potential pathogens from cellulitis aspirates is only 25-35%. A decubitus swab provides little clinical information and a tissue biopsy or needle aspirate is always to be preferred. The same applies to superficial tissue samples of gangrenous tissue. For otitis externa, vigorous swabbing is required, because surface swabbing may miss streptococcal cellulitis.

For **anaerobes**, the specimen collection method must preclude contamination by anaerobic flora of mucocutaneous surfaces. Specimen transportation must avoid excessive exposure to air. Valid specimens are blood cultures; aspirates of closed spaces such as pleural fluid, peritoneal fluid, ascitic fluid, joint fluid, cerebrospinal fluid; specialised procedures that bypass mucocutaneous surfaces, such as transtracheal aspiration, direct lung aspirate, protected bronchoscopic brushing, suprapubic bladder aspiration, culdocentesis; deep aspiration of wounds and loculated abscesses; surgical specimens and tissue biopsies from any normally sterile site; Bartholin's gland; bile; bone marrow; Fallopian tube; intrauterine device for *Actinomyces*; ovary; placenta via caesarean section; sinus aspirate; stool for *Clostridium*; swab or tissue from surgical wound; endometrial aspirate from uterus.

The most practical and efficient system of **swab transport** for bacteriological systems is the use of cotton wool swabs pretreated with Sorensen's buffer placed in SIFF medium. Stuart or Amies medium may also be used. Even with transport medium, delays of > 1 h in transit of wound swabs, sputa, tracheal aspirates and urine can cause alterations to the microbial flora and loss of clinically significant species. *Trichomonas vaginalis* will remain viable for ≈ 24 h on dacron swabs transported in Amies medium.

Pathogenic ***Neisseria*** are particularly sensitive to cold, heat and lack of CO_2.

For **genital lesions**, a swab and slide of transudate from the base of the lesion is the preferred specimen.

Great care should be taken to avoid loss of a **minute biopsy or corneal scraping.**

Swabs for **viral culture** must be collected directly into viral transport medium (Virocult (Medical Wire) is the most efficient system). Stuart's transport medium rapidly inactivates most viruses, and calcium alginate swabs should not be used. Swabs for herpes should be refrigerated rather than frozen. *Human cytomegalovirus* and *simplexvirus* virus are routinely isolated from cervical, urethral and vaginal swabs; *molluscum contagiosum virus* and *human papillomavirus* are not cultivable. Adenovirus, *coxsackievirus A*, *human cytomegalovirus*, *simplexvirus*, *human enterovirus 70* and *Newcastle disease virus* are routinely isolated from conjunctival swabs. Influenza virus, parainfluenza virus, *Rhinovirus* and *respiratory syncytial virus* are routinely isolated from nasal and nasopharyngeal swabs, aspirates or washings, though influenza virus and *respiratory syncytial virus* are usually detected by antigen assay (ELISA or EIA). Adenovirus, *human cytomegalovirus*, enterovirus, *simplexvirus*, influenza virus, *measles virus*, *mumps virus* and parainfluenza virus are routinely isolated from throat swabs; *respiratory syncytial virus* may also be isolated by non-routine methods. Adenovirus, *Enterovirus*, *measles virus* and *human rubella virus* are routinely isolated from swabs taken from the base of maculopapular rash lesions, while

coxsackievirus A, echovirus, *simplexvirus* and *human herpesvirus 3* are similarly isolated from vesicular rashes (vesicle aspirate in viral transport medium preferred for varicella-zoster). Poxviruses may be isolated from similar specimens by non-routine methods. Exudates, cellular scrapings and washings should be collected into buffered tryptose phosphate broth with gelatine or Hank's balanced salt solution with gelatine. Adenovirus, *human cytomegalovirus* (collect 2 or 3 specimens on successive days), *simplexvirus* and *mumps virus* are routinely isolated from urine, while *JC polyomavirus* and *human rubella virus* may be isolated by non-routine methods. Urine and throat washings for *human cytomegalovirus* should be held in 70% sorbitol. Other specimens should be refrigerated or frozen. All specimens should be processed within 3 hours if possible. Viral and chlamydial tests require separate collection and transport kits.

Gastric aspirates or washings for mycobacteria must be processed (neutralised) promptly.

The use of transport media with **feces** provides little benefit, either for culture or for parasitological examination. Speed of transport and prevention of drying and extremes of temperature are more important factors. If it is desired to use a preservative to transport feces for parasitology, sodium acetate-acetic acid-formalin is probably the best single agent, though albumen-coated slides are required. Specimens for parasites must not be contaminated with urine or water, dried out, or contain bismuth, barium, magnesium, mineral oil or gallbladder dye (requires 21 d clearance). Adenoviruses and enteroviruses are routinely isolated from feces; *Rotavirus* is usually detected by enzyme immunoassay.

Rectal swabs should be reserved for detecting gonorrhoea (specimen taken from anal crypts, avoiding feces as much as possible) or for *Shigella* or *Campylobacter* (feces must be seen on swab) in patients unable to provide feces or for *simplexvirus* or rectal carriage of group B streptococci.

The proper timing of **specimens for serology and antibiotic serum assay** should be carefully observed.

In the laboratory, the value of **each specimen** should be carefully evaluated and poor quality or unnecessarily duplicated specimens not processed.

Chapter 25

Microscopy

Smear Preparations

Acid-Fast Bacilli: 5% phenol in ethanol fixed Kinyoun and Truant's fluorochrome, modified Ziehl-Neelsen stain
Anaerobes: heat fixed Kopeloff
Bacteria: heat fixed Gram, alcohol/acetone fixed direct immunofluorescence
Bacterial Flagella: basic fuchsin-tannic acid flagellar stain
Candida: 0.0025% calcofluor in peptone/glucose medium (germ tubes and morophology)
Chlamydia: alcohol/acetone fixed direct immunofluorescence, heat fixed Gimenez, glutaraldehyde fixed electron microscopy
Corynebacterium: Loeffler's methylene blue stain, Albert's stain, Neisser's stain
Cryptococcus: nigrosine negative stain wet preparation, India ink wet preparation, 10% formalin fixed mucicarmine stain
Cryptosporidium: Sheather's wet preparation, modified Ziehl-Neelsen stain, immunofluorescence
Feces: saline wet preparation, iodine stain wet preparation, MIF stain wet preparation, Schaudinn's fixed trichrome stain; look for leucocytes, erythrocytes and parasites (particularly trophozoites) in mucus strands if present (particularly with formed specimens)
Fungi: KOH-Parker Quink wet preparation, lactophenol cotton blue wet preparation, calcofluor white wet preparation, alcohol/acetone fixed direct immunofluorescence, 10% formalin fixed periodic acid-Schiff, Gridley and Grocott's methenamine silver stain
General Morphology: saline wet preparation
Giardia: zinc sulphate flotation or formalin-ether wet preparation
Histopathology: 10% formalin fixed haematoxylin and eosin stain
Histoplasma: Giemsa stain
Legionella pneumophila: 10% formalin fixed Dieterle silver, immunofluorescence (direct and indirect)
Leucocytes: methylene blue wet preparation, Romanowsky stain
Mycobacterium: acid-fast stain
Mycoplasma: Dienes stain wet preparation
Nocardia: 10% formalin fixed Gram-Weigert, acid-fast stain
Parasites: iodine and formalin-ether wet preparations, unfixed dried Wright stain, alcohol/ether fixed Giemsa and direct immunofluorescence, Schaudin's fixed trichrome
Pneumocystis jirovecí: unfixed dried toluidine blue 0
Prototheca: Grocott's silver stain, PAS
Rickettsia: heat fixed Gimenez
Schistosoma: 10% formalin fixed modified Ziehl-Neelsen stain
Toxoplasma qondii: immunoperoxidase stain
Treponema: darkfield wet preparation
Viruses: electron microscopy and immune electron microscopy of unfixed negative stained wet preparations and glutaraldehyde fixed dried preparations, alcohol/ether fixed Papanicolaou and indirect immunofluorescence

Gram Stain

Amies transport medium and culture collection devices have been associated with false positive Gram stains.

The importance of the Gram stain in determining the quality of a sputum specimen (absence of squamous epithelial cells, absence of mixed normal flora, presence of histiocytes) and in identifying likely pathogens present should not be underestimated. The isolation of a light growth of an organism which has not been seen in a Gram stain is unlikely to be of significance unless there is a virtual absence of other organisms and the patient has been on antibiotics. *Haemophilus* requires at least a minute of counterstaining with safranin and is in any case frequently difficult to see in Gram stains of sputum. Unless the patient is hospitalised, bed-ridden, alcoholic or immunocompromised, and/or the Gram stain shows clear evidence of a lower respiratory tract specimen in which the organism is present together with a significant number of neutrophils, coliforms and non-mucoid strains of *Pseudomonas* can safely be ignored.

A Gram stain of faeces is useful in diagnosing enterocolitis. In both *Staphylococcus aureus* and *Campylobacter jejuni* infections, specimens will typically contain large numbers of leucocytes and erythrocytes. In the case of a *Staphylococcus aureus* infection, the Gram stain will show large numbers of Gram positive cocci, usually recognisably staphylococci; mannitol salt agar may be used as an isolation medium. In *Campylobacter jejuni* infections, the 'squiggly' Gram negative bacilli may be seen in a Gram stain; microaerophilic culture at 42°C is necessary.

In plague infections, the presence of bipolar staining Gram negative rods in lymph node aspirate can be diagnostic.

The search for anaerobic bacteria begins with the direct examination by Gram stained smear. This technique provides immediate information regarding the types of organisms present and may be sufficient to permit a presumptive diagnosis and choice of therapy.

Pseudomonas and Enterobacteriaceae may be differentiated in Gram stained direct smears.

In CSF, a Gram stain detects between 10^5 and $\geq 10^7$ cfu/mL of both Gram positive and Gram negative organisms in $<$ 5 minutes. There is a 75-80% correlation with culture.

A Gram stain detects urinary tract infections in 2 minutes, with a sensitivity of 97% at 10^5 cfu/mL (decreased sensitivity at $< 10^5$ cfu/mL).

The Gram stain serves as a quality control. Organisms corresponding to all the types seen in the Gram should be cultured.

Methanol fixation is superior in every instance to heat fixation and should especially be used for specimens, such as CSF and synovial fluid, containing large amounts of protein.

Chapter 26

Culture

Suitable Media For Specific Organisms

***Acanthamoeba*:** 1.5% agar with *Escherichia coli*

***Actinobacillus*:** blood agar CO_2 + moisture

***Actinomyces*:** blood agar + vitamin K and blood agar + colistin and nalidixic acid anaerobic + CO_2 (enriched thioglycolate broth suitable only for pure cultures)

Adenovirus: oropharyngeal, nasopharyngeal, throat gargle, throat swab, faeces, conjunctival swab, sputum in HEP2, embryonic kidney cells

***Aeromonas*:** blood agar + 10 mg/L ampicillin, MacConkey agar, SS agar

***Alcaligenes*:** MacConkey agar

Anaerobes: CDC anaerobic blood agar, phenylethyl agar, vancomycin kanamycin agar (Gram negative), paromomycin vancomycin blood agar (Gram negative), enriched thioglycolate broth. Selective media should always be used for isolation, since only 61% of Gram negative and 73% of all anaerobes will be isolated on non-selective media. Using an anaerobic jar, within 30 minutes it is possible to check the system is working by reduction of methylene blue indicator from blue to white, condensation on surface of jar and jar becoming warm. Palladium catalysts are readily inactivated by excessive moisture and H_2S.

Anaerobic Streptococci: sheep blood agar with neomycin

Arbovirus: blood, brain post mortem in chick embryo chorioalantoic membrane or yolk sac, cell culture

Avian Bronchitis-like Virus: throat swab or washings in diploid human embryonic fibroblasts, organ culture of trachea or nasal epithelium

***Bacillus*:** blood agar aerobic

***Bacteroides*:** sheep blood agar with kanamycin and vancomycin anaerobic

***Bordetella*:** blood agar (some species), Bordet-Gengou potato-glycerol blood agar, charcoal agar with antibiotics in moist atmosphere

***Brucella*:** blood agar CO_2

***Campylobacter*:** enrichment in medium of Martin et al, Skirrow's medium microaerophilically at 42°C

***Capnocytophaga*:** blood agar CO_2

***Cardiobacterium hominis*:** blood agar CO_2 + moisture

***Chlamydia*:** McCoy's tissue culture with Stoxil

***Chromobacterium violaceum*:** MacConkey agar, SS agar

***Clostridium*:** blood agar anaerobic, cooked meat medium

***Clostridium difficile*:** feces on blood agar + cycloserine + cefoxitin + fructose anaerobic

***Clostridium perfringens* (foodborne illness):** feces and food on tryptose sulphite cycloserine agar anaerobic

***Corynebacterium*:** blood agar, cysteine tellurite blood agar, Loeffler's serum, Tinsdale aerobic

Coxsackievirus: feces, throat swab, CSF, heart post mortem in monkey or human cell culture

Diphtheria: throat membrane fragments on Tinsdale, Loeffler's

Echovirus: feces, throat swab, CSF in monkey or human cell culture

***Eikenella corrodens*:** blood agar CO_2

***Entamoeba*:** Balamuth's, egg yolk medium

Enterobacteriaceae: MacConkey, eosin methylene blue

Enterohemorrhagic *Escherichia coli*: 0.5% sorbitol MacConkey agar

***Escherichia*:** MacConkey or eosin methylene blue aerobic

***Erysipelothrix rhusiopathiae*:** blood/glucose agar CO_2

***Francisella tularensis*:** nodules, pustules, ulcers, lymph node aspirate, blood, pleural aspirate, sputum on glucose-cystine-thiamine blood agar, cystine-heart blood agar, cystine-yeast agar + α-ketoglutarate, chocolate agar + Isovitalex, Thayer-Martin medium aerobic

Fungi: Sabourand, Mycosel, brain heart infusion, malt extract agar; requirements include detailed clinical notes, adequate amount of suitable clinical material, thorough direct microscopic examination of potassium hydroxide-ink mounts or stained smears, histopathology of biopsy tissue stained with special fungal stains, and use of antibacterials in primary isolation media

***Fusobacterium*:** blood agar anaerobic

Gardnerella vaginalis: heart infusion agar + 6% rabbit or human blood CO_2

Haemophilus: enriched chocolate agar CO_2

Haemophilus ducreyi: enriched chocolate agar + 1% bovine haemoglobin + 5% serum, Muller-Hinton agar + 5% chocolatised horse blood in high humidity at 33-35°C

Helicobacter pylori: multiple gastric mucosal biopsies on chocolate agar or brain heart infusion agar ± nalidixic acid (50 mg/L), vancomycin (3 mg/L) and trimethoprim (5 mg/L) aerobic + CO_2 + moisture

Human cytomegalovirus: saliva, throat swab, urine, leucocytes, liver, etc in human embryonic fibroblasts

Human papillomavirus: organ culture of infected skin treated with TPA to increase keratinocyte differentiation

Human rubella virus: throat swab, blood, urine, any organ of rubella babies in RKI3, BHK21, green monkey kidney, rabbit cornea

Influenza: oropharyngeal, nasopharyngeal, throat swab or gargle specimens, lung tissue post mortem in chick embryo amnion, human, monkey, pig or calf kidney

Klebsiella: MacConkey or eosin methylene blue

Klebsiella granulomatis: egg yolk-containing media aerobic

Lactobacillus: special medium anaerobic + CO_2

Legionella: ACES-buffered charcoal yeast extract medium + α-ketoglutarate (BCYEα) and BCYEα + cephamandole + polymyxin B + anisamycin (BMPAα) or BCYEα + glycine + vancomycin + polymyxin B + anisamycin (MWY)

Leishmania: Novy McNeil Nicolle medium, hamster inoculation

Listeria: previous storage of specimens at 4°C, enrichment in broth based on trypticase ± peptones + acriflavine dyes + nalidixic acid ± potassium thiocyanate ± cycloheximide, blood agar, blood agar + cycloheximide + colistin + cefotetan + fosfomycin +acriflavine aerobic

Marburgvirus: blood, serum, suspensions of heart, kidney, liver, spleen in Vero cells

Micrococcus: blood agar aerobic

Morbillivirus: throat swab, blood, brain or lung post mortem in human kidney or amnion cells

Mumps virus: saliva, CSF, urine in monkey or human kidney, chick embryo amnion

Mycobacterium: Lowenstein-Jensen, Gruft, Middlebrook 7H9, 7H10, 7H11, selective 7H11, Dubos, Wallenstein aerobic, isolator lysis centrifugation or other concentrate to Bactec 7H12, 13A

Mycoplasma: modified SP-4 broth and A7B agar

Neisseria: blood agar, chocolate agar, Thayer-Martin, Transgrow, New York City CO_2

Nocardia: blood agar, chocolate agar, mycobacterial media, modified Thayer-Martin medium, paraffin-containing medium, BMPAα, MWY charcoal yeast extract agar aerobic

Orf virus: vesicle fluid or pus in chick embryo chorioallantoic membrane

Parainfluenza: oropharyngeal, nasopharyngeal, throat gargle, sputum in monkey or human kidney cells

Pasteurella: blood agar aerobic (except *P.aerogenes*—obligate anaerobe)

Pertussis: nasopharyngeal swab on charcoal agar + antibiotics

Plesiomonas shiqelloides: MacConkey agar, SS agar

Pneumocystis jiroveci: Vero cell culture

Pneumovirus: throat swab, sputum in HEP2 cells

Poliomyelitis: throat swab, stool in monkey or human cell culture

Proteus: blood agar, MacConkey aerobic

Pseudomonas: blood agar, MacConkey aerobic

Reovirus: feces, throat swab in monkey kidney cells

Rhinovirus: nose or throat swab in diploid human embryonic fibroblast culture at 33°C and pH7

Rickettsia: embryonated egg

Rotavirus: differentiating human colon carcinoma cell line + trypsin

Salmonella: enrichment in Gram negative broth or selenite broth, xylose lysine desoxycholate agar, MacConkey, SS agar aerobic

Shigella: enrichment in gram negative broth, xylose lysine desoxycholate agar, MacConkey, eosin methylene blue, SS agar aerobic

Simonsiella: sheep blood agar, BSTSY agar aerobic

Simplexvirus: vesicle fluid, throat swab, CSF, corneal scraping, brain post mortem in any cell culture (Cellmatics mink lung cells, MRC-5 most useful; shell vial centrifugation enhancement fastest and most sensitive procedure), chick embryo chorioallantoic membrane or yolk sac

Spirillum minus: animal inoculation

Staphylococcus: blood agar, mannitol salt agar aerobic

Streptobacillus moniliformis: blood agar aerobic + moisture

Streptococcus: blood agar anaerobic + CO_2
Streptomyces: blood agar aerobic
Trichomonas: Ruperberg broth
Trypanosoma: Novy McNeil Nicolle medium
Ureaplasma: modified SP-4 broth and A7B agar
Varicellovirus: vesicle fluid in human embryonic fibroblasts
Veillonella: selective media with lactic acid
Vibrio: alkaline media, thiosulphate citrate bile sucrose agar, sucrose teepol tellurite agar, most common media containing 0.5-1% salt
Yersinia: cold enrichment, blood agar aerobic, cefsulodin-irgasan-novobiocin medium

General Notes For Reading Cultures

The first step is to read the request form, noting especially if the referring clinician has made any special requests, if the patient is on any antimicrobial therapy, any previous culture results, and the patient history (including immunocompromise and hospitalisation).

The result of the primary Gram stain should be consulted, noting the number and types of cells present and assessing whether the organisms seen in the Gram stain have grown on culture and vice versa. If Gram stain and culture do not correlate, the Gram stain should be checked and amended if necessary or a further effort made to isolate organisms seen which have not been cultured (eg, prolonged incubation, reinoculating specimen onto more appropriate media).

Culture plates should be read in conjunction with each other, noting, for example, whether organisms growing on blood agar also grow on MacConkey or colistin nalidixic acid agar, whether organisms growing on anaerobic plates are also growing on aerobic plates, whether haemolysis differs on blood agar and *Gardnerella vaginalis* agar.

All plates from cutaneous wounds that have moderate to numerous leucocytes seen in the Gram stain and no pathogen isolated should be reincubated for 5 days to check for *Mycobacterium* or *Nocardia.* If a patient has chronic ulcers and nothing has been isolated from previous swabs received, these plates should be reincubated also.

Suitable Media For Specific Sites

Respiratory Specimens: Blood agar grows most significant aerobic respiratory flora except *Haemophilus influenzae,* which will grow but usually only as tiny colonies. It is important that the medium used shows the correct haemolysis. **Enriched chocolate agar + bacitracin** grows *Haemophilus influenzae* well, the bacitracin inhibiting Gram positive organisms, though some *Haemophilus influenzae* strains are also sensitive to it. **Colistin nalidixic acid agar** grows Gram positive, but not most Gram negative, organisms and can be useful with sputa containing enteric Gram negative bacilli and *Pseudomonas.* In patients where they are likely to be significant, enteric Gram negative bacilli and *Pseudomonas* can be isolated on **MacConkey agar.** Where appropriate, cultures for *Mycoplasma* can be set up on **A7B agar.**

Feces: Xylose lysine deoxycholate medium relies on xylose fermentation, lysine decarboxylation and production of H_2S for primary differentiation of *Salmonella and Shigella* from non-pathogenic bacteria. Sodium desoxycholate is included to inhibit conforms. ***Salmonella shigella*** **agar** contains bile salts to inhibit Gram positive organisms and coliforms and relies on lactose fermentation for primary differentiation. **CIN medium** contains an antibiotic supplement and sodium desoxycholate to select for *Yersinia enterocolitica.* **Skirrow's medium,** consisting of blood agar + vancomycin, polymyxin B and trimethoprim, is incubated at 42°C under microaerophilic conditions for the selective isolation of *Campylobacter.* Liquid specimens, or specimens submitted with a history of food poisoning after ingestion of seafood, should be screened for *Vibrio* using **thiosulphate citrate bile sucrose agar,** on which they produce colonies > 2 mm after 24 h incubation. ***Clostridium difficile*** **agar** consists of blood agar + D-cycloserine and cefoxitin, which inhibit almost all other organisms. The organism should be screened for if there is a history of diarrhoea following use of antimicrobials. Plates are incubated at 37'C anaerobically for 48 h. If *Aeromonas* is suspected, it may be cultured on **blood agar + ampicillin.**

Urine: Cystine lactose electrolyte deficient medium supports the growth of all urinary pathogens (with rare exceptions), giving good colonial differentiation and clear diagnostic characteristics. The presence of important contaminants, such as diphtheroids, *Lactobacillus and Micrococcus,* is also clearly elicited, giving an indication of the degree of contamination. It provides a non-inhibitory diagnostic agar for plate culture of urinary organisms. It is electrolyte deficient to prevent the swarming of *Proteus.* Suprapubic aspirates, ureteric specimens and other urines for which more extensive treatment is warranted may also be cultured onto enriched chocolate agar, anaerobic media and into thioglycolate broth.

Genital Specimens: Blood agar will grow most aerobes found in genital specimens, exceptions being *Neisseria gonorrhoeae,* which grows poorly after 48 h (*Neisseria meningitidis* grows well after 24 h), and *Haemophilus influenzae,* which grows poorly unless *Staphylococcus* is present, in which case satellitism may be observed (note that other organisms also produce satellitism). **Enriched chocolate agar + bacitracin** should be set up on females less than 10 years old in case of a *Haemophilus influenzae* infection. **New York City medium** contains lincomycin to inhibit Gram positive cocci, amphotericin B to inhibit yeasts, and colistin and trimethoprim to inhibit Gram negative bacilli, and is designed to grow only pathogenic *Neisseria.* However, yeasts and *Enterococcus faecalis* often grow. ***Gardnerella vaginalis*** **agar** contains nalidixic acid to inhibit staphylococci, amphotericin B to inhibit yeasts and gentamicin to inhibit Gram negative

bacilli, and grows *Gardnerella vaginalis*, streptococci and *Lactobacillus.* **MacConkey agar** grows Gram negative bacilli and *Enterococcus faecalis*. **Blood agar + vitamin K** will grow all anaerobes. The use of a metronidazole disc on the plate will help to distinguish true anaerobes (nearly all sensitive to metronidazole) from facultative anaerobes (resistant to metronidazole). Gram negative anaerobes can be cultured on **blood agar + vancomycin and kanamycin.** Vancomycin inhibits Gram positives and kanamycin facultative aerobic Gram negatives. *Candida albicans* will grow and *Enterococcus faecalis* will sometimes grow on aged media.

Chapter 27

Identification of Isolates

Background

The identification of a bacterial isolate involves deciding whether or not its properties are similar enough to those of a described species for it to be considered identical with that species. This depends, of course, on the particular classification adopted.

Most organisms are classified almost solely on morphological criteria, but classifying bacteria into *Bacillus, Micrococcus* and *Spirochaeta* doesn't get us very far, so such things as atmosphere required for growth, staining properties and biochemical tests are used.

It was soon realised that characteristics for classification should be as correlated with other characteristics as possible. This means that some characteristics can be used as key characteristics to rapidly identify an organism—eg, rapid indole production for *Escherichia coli*. It also led to the widespread use of keys for identification. However, this approach has its problems: real exceptions occur to most characteristics for most organisms, supposed key characteristics may be shared by quite dissimilar organisms while varying for quite similar ones, and slight variation in technique can cause wrong results and wildly incorrect identifications.

Numerical taxonomy takes an entirely different tack: testing organisms for a large number of characteristics, each of which is given equal weight, and classifying them in clusters of similarity, which form natural taxons. This approach forms the basis of such systems as the API and the various Vitek cards. The 20 or so characteristics chosen for each system were those which had been found to be both highly correlative and most constant for the group of organisms for which the system was designed. These systems now constitute the mainstay of bacterial identifications in the clinical laboratory, but key reactions, many using commercial packages, are also frequently used. For many of those organisms for which no simple packaged system exists, tables and/or keys are available which enable identification.

Genetic methods of classification and identification are making their appearance. These are sometimes useful. Unfortunately, however, genetic classifications are often not very useful clinically. For example, genetically, *Escherichia coli* and *Shigella* should be in the same species.

The Approach to the Identification of Bacteria in the Medical Laboratory

The importance of knowledge and experience and the consequent 'feel' for a bacterial species cannot be overemphasised. If you know the growth characteristics of an organism, its appearance, smell (if any), perhaps a few key biochemical reactions, likely antibiogram, its usual habitat and the circumstances under which it is likely to be isolated in a clinical laboratory, the identification can be rapid and you are unlikely to be misled into error.

Most clinical specimens are seeded to a number of different types of media and it is important to compare the growth on the different media. For example, an organism growing on blood agar but not enriched chocolate agar with bacitracin is probably Gram positive; one growing on enriched chocolate agar with bacitracin but not on blood agar (except, perhaps, as pinpoint colonies) is probably *Haemophilus*; one growing on blood agar and colistin nalidixic acid agar but not MacConkey is Gram positive; one growing on blood agar, colistin nalidixic acid agar and MacConkey is likely to be either *Enterococcus faecalis* (tiny colonies) or a *Pseudomonas* species; one growing on blood agar but not colistin nalidixic acid agar or MacConkey is probably a non-Enterobacteriaceae Gram negative; etc.

Speed of growth can also be a useful clue. A Gram positive rod appearing overnight, or even in 48 hours, is definitely not a *Mycobacterium*. On the other hand, a *Haemophilus* that takes 48 hours to make a feeble growth on enriched chocolate agar from an eye swab may well be suspected of being *Haemophilus aegyptius* rather than *Haemophilus influenzae*.

Use of colonial characteristics as a criterion has fallen into disfavour in many identification systems. This is largely because such characteristics are difficult to describe in terms that mean the same to all observers, impossible to include in numerical type taxonomies and even difficult to incorporate into keys and tables. However, many bacteria regularly produce colonies that are typical and almost instantly recognisable, reducing identification procedures to one or two simple confirmatory tests, such as Staphyslide for *Staphylococcus aureus* and indole for *Escherichia coli*. Equally, if an identification system gives you an identification which does not accord with the appearance of the organism as you know it or as it is described in the texts, you should seriously question that identification.

Similar remarks can be made for smell. As proved in a survey with *Streptococcus milleri*, the smell of the growth of some organisms is so characteristic as to approach an absolutely reliable identification procedure.

The Gram stain reaction remains probably the single most correlative characteristic of an organism. This is despite the fact that isolates of some supposedly Gram positive species frequently stain Gram negative. Correlation with the colonial appearance and with the type of media on which the organism is growing may prevent an error in some cases. Also, in many cases, one can learn to recognise microscopically the morphology of species such as *Bacillus* and *Lactobacillus* which

frequently overdecolorise, and even to detect the minute difference in the appearance of the cell wall in Gram positive and Gram negative species. The potassium hydroxide string test [Place colony in 3% potassium hydroxide and lightly emulsify. Slowly draw out wire. Gram negatives will form a string from solution to wire.] is a useful supplement in doubtful cases. Unfortunately, it is not infallible, and *Achromobacter*, *Acinetobacter*, *Agrobacterium* and *Moraxella* regularly give false negative reactions, while *Bacillus* species may give a false positive. Where suspicion still exists, vancomycin susceptibility may settle the question; all Gram positives except *Lactobacillus*, *Leuconostoc*, *Pediococcus* and rare strains of *Enterococcus* are sensitive, while *Acinetobacter* and *Moraxella* are the only Gram negatives which may show sensitivity. Nalidixic acid and polymyxin susceptibility also correlate very well (though not perfectly) with 'true' Gram stain reaction—Gram positives are resistant, and Gram negatives susceptible, to both. Again, an oxidase negative and/or large-celled Gram negative bacillus which is penicillin susceptible should be viewed with suspicion unless it has been identified as belonging to a species which includes penicillin susceptible strains.

Slow-growing Gram positive bacilli of fine morphology should be subjected to a modified Ziehl-Neelsen stain.

The actual morphology of an organism is frequently characteristic and can sometimes be virtually diagnostic. It is important not to minimise the usefulness of this information. In some cases, it may be difficult to decide if an organism is a rod or a coccus. The appearance of cells grown in the presence of a β-lactam to which they are susceptible (eg, from the zone edge around a penicillin disc) can often be useful in deciding this; cocci tend to enlarge and disrupt spherically, while rods are prone to elongate.

Other important properties that can be almost instantly determined are the catalase and oxidase (Kovacs method using a platinum (never nichrome) loop to inoculate an 18-24 hours old colony from a non-selective and non-differential medium to freshly prepared 1% tetramethyl-p-phenyldiamine dihydrochloride (reacts with cytochrome c to form a blue coloured compound; positive reaction must occur in 10 seconds) is the most satisfactory method) reactions. Motility may also be apparent in a simple wet preparation.

The single most important biochemical characteristic is undoubtedly the O-F reaction. Whether an organism utilises glucose fermentatively, oxidatively or not at all is a highly correlative criterion. For most organisms, Hugh-Leifson's medium should be used for the purpose. [Hugh-Leifson medium differs from carbohydrate fermentation media by decrease of peptone concentration from 1% to 0.2%, increase of carbohydrate concentration from 0.5 to 1% and decrease of agar concentration from 0.3% to 0.2%.] However, for more fastidious organisms, such as coryneforms, *Neisseria*, *Moraxella*, etc, it may be necessary to use cysteine tryptone agar sugars to establish this criterion. It is important to realise that nonfermentative organisms are strict aerobes and vice versa.

Given just the above criteria, Cowan and Steele's initial tables purport to group all the bacteria one is likely to encounter in a clinical microbiology into a number of groups which lead on to further tables eventually allowing a firm identification. In many cases, this is true. However, blindly following the scheme can readily lead one into error. This is because of the broad groupings, with lack of due notice given to important exceptions; the fact that absolute positive and negative values of characteristics are given at the 85% level, which gives a fairly high probability of encountering an exception; because descriptions of genera are sketchy and sometimes wrong in failing to note important exceptions, while descriptions of species are virtually nonexistent; such basic properties as colonial and cellular morphology are rarely mentioned. So, anyone using Cowan and Steel should check the identification carefully against a description in Balows or Bergey.

The tables in Balows are more complete, frequently quote percentages, and are usually accompanied by clear descriptions of species. The problem with Balows is that it largely presupposes enough knowledge to be able to get to the right table. The three keys—'Nonenterobacteriaceae Fermentative Gram Negative Bacilli', 'Non-fermenting Gram Negative Bacilli' and 'Fastidious Gram Negative Bacilli'—require only urea, indole, nitrate and lactose as additional tests and are very useful but there are problems getting there: How do you know a fermentative Gram negative bacillus is non-Enterobacteriaceae? Why isn't *Pseudomonas* in 'Non-fermenting Gram Negative Bacilli'? Why does 'Fastidious Gram Negative Bacilli' not include *Haemophilus*, *Brucella*, etc?

Probably the best scheme for identification of nonfermenting and fastidious Gram negative bacilli is the Weaver-Hollis scheme. However, even here there are problems: misread any one of the three prime separating criteria (O-F, MacConkey, oxidase) and you'll quickly be right off the track; many of the tests are not ones normally used in the laboratory; some organisms are far more quickly and definitively identified by alternative procedures; referral to fuller descriptions of organisms is still required.

The packaged identification systems, such as Vitek and API, can be extremely useful if used within their limitations, but it is essential to know what the limitations of each of these systems are. These limitations can arise because the necessary data are not in the data base, because the tests employed have insufficient discrimination for particular organisms, or because a test gives incorrect results. All these systems should be used strictly as directed. Eg., reading an API before 14 hours can definitely give false results, as can employing the wrong inoculum density in the Vitek. It is possible to use reactions obtained in these systems to 'manually' identify organisms. However, a great deal of caution must

be applied here since different results may well be obtained using different methods—something that must be borne in mind whatever method you are using. Reactions obtained after prolonged incubation (> 12 h) in the GNI cannot be trusted.

[**API20E:** With the API20E, the basic inoculation time is 14-24 hours. Attempts to read results earlier will frequently result in misidentification. It is always wise to set up the standard extra tests (motility, nitrate, O-F glucose, MacConkey) on any oxidase positive organism; also, any organism which shows only a few reactions after overnight incubation should be reincubated for a further 24 hours and the extra tests set up. The API20E correctly identifies about 93% of common Enterobacteriaceae. The identification of any organism by the API20E must be critically regarded, particularly when it is based on only a few characteristics. In inoculating the API20E, a single well-isolated colony suspended in 5 mL saline should be used. For organisms which do not grow on MacConkey or on the usual susceptibility test agars, the addition of a few drops of sterile serum to the saline will improve the test. A purity plate should be set up from the suspension inoculated. Though API literature suggests performing oxidase and nitrate tests on the strip, these are much better performed externally: the oxidase test using the Kovacs oxidase test on filter paper, the nitrate test in a tube of nitrate broth. [In reading the nitrate test, a red colouration (diazo dye complex) on the addition of the nitrate A (sulphanilic acid) and B (α-napththylamine) reagents indicates reduction of nitrate to nitrite. If no red colouration appears, add a small amount of zinc dust; a red colouration indicates no reduction of nitrate, while no red colouration indicates reduction of nitrate to nitrogen gas.] The API32E is virtually 100% accurate for common Enterobacteriaceae, but the API10S correctly identifies only about 70%. It may be worth noting that, except for the gelatinase reaction, all the tests utilised in the API20E are readily adapted to a self-prepared microtitre formula, which should give excellent agreement ($\approx$ 97%) with results obtained using the commercial system.

Replicator Techniques may be used in identification, giving a 95% correlation with API20E.

Identification of Nonfermentative and Oxidase Positive Fermentative bacteria: Commercial systems are not particularly reliable, the Oxi/Ferm system being 80% accurate, the Minitek 72% and the API20E 61%. However, failure is usually due to a failure of generated codes to appear in the compendium, rather than of misidentification. These systems can still be usefully employed if used very critically.

Vitek: The Vitek can identify a variety of Gram negative and Gram positive organisms in 3-13 hours and perform susceptibility testing in 3-10 hours (4% very major errors). Identification of common Enterobacteriaceae is virtually 100% accurate. Vitek 1 accurately identifies *Burkholderia pseudomallei* but Vitek 2 does not. Direct identification and susceptibility testing of a suspension of centrifuged organisms from positive blood cultures is possible in many cases (93% accuracy overall); however, it will not work with such organisms as pneumococci, *Neisseria* and *Haemophilus* and may give erroneous results for oxacillin sensitivity of *Staphylococcus aureus*, several antimicrobial agents with enterococci, and ampicillin and cephalosporins with *Citrobacter*, *Enterobacter* and *Serratia*..

Other Systems: Of the other common systems, Microscan correctly identifies about 98% of common Enterobacteriaceae, Microbact 24 about 90%, Microbact 12 about 57%, and BBL Crystal about 79%.

The identification of fecal isolates is usually a matter of following a simple protocol, which will allow the identification of virtually all likely significant isolates. The rapid SST strip is a rapid, accurate and cost-effective method of enteric pathogen screening.

On xylose lysine deoxycholate medium, *Salmonella* appears as distinct black colonies due to H_2S production, and on Salmonella-Shigella agar as clear colonies with some H_2S production. Test first for urease production [converts urea to ammonium carbonate, giving an alkaline reaction; spot test positive in 2 minutes, tube test in 2 hours or less]. If positive, this is not *Salmonella* (probably *Proteus*). If urea negative, identify the isolate using the Vitek or API system. Also set up a nutrient agar plate for agglutinations. A heavy suspension is made of the suspected *Salmonella* in formal saline from the nutrient agar plate. To drops of this suspension are added 1 drop of polyvalent A-G and/or polyvalent A-S (somatic O antigens), polyvalent H (flagellar antigen) and Vi (capsular antigen) respectively. If polyvalent A-G and/or A-S and polyvalent H are positive and Vi negative, the organism is a *Salmonella* other than *Salmonella typhi* and can be further identified by specific agglutinations. If the somatic O antigens are negative, the suspension should be boiled and the agglutinations repeated. If the Vi reaction is positive, boil the suspension for 15 minutes and repeat the agglutinations. *Salmonella typhi* will agglutinate in poly H and Vi but usually not polyvalent O or group D specific sera before heating (VW strains will agglutinate in both Vi and group D without heating; the heating destroys the capsular (Vi) antigen which masks the somatic O antigen).

Shigella does not ferment xylose and appears as red, sometimes crenated, colonies on xylose lysine deoxycholate agar, clear on Salmonella-Shigella agar. *Shigella* is usually associated with leucocytes and erythrocytes in the feces. It may be identified using the Vitek or API.

Colonies of *Aeromonas hydrophila* are large, rhizoid, non-xylose fermenting and oxidase positive. When subcultured onto blood agar, they are β-hemolytic. Identification is by Vitek or API.

Plesiomonas shigelloides is non-xylose fermenting, oxidase positive, non-haemolytic on blood agar. Identification is by API or Vitek.

Campylobacter is a microaerophilic Gram negative bacillus which grows at 42°C. On Skirow's medium (blood agar with vancomycin, polymyxin B and trimethoprim), the colonial morphology ranges from small discrete colonies through to swarming colonies which may cover the entire surface of the plate in a uniform film and can be easily missed. *Campylobacter* is oxidase and catalase positive and appears in a Gram stain as Gram negative delicate 'seagull-like' rods. Rapid hippurate discs are used to differentiate between *Campylobacter jejuni* (positive) and other thermophilic *Campylobacter* species (negative).

Typical colonies of *Yersinia enterocolitica* on CIN medium are small, dark red colonies with a clear border, usually ≤ 1 mm. On xylose lysine deoxycholate medium they appear as tiny clear colonies. A rapid screening test using urea/phenylalanine deaminase discs can be performed (urea positive, phenylalanine deaminase negative organisms are presumptive *Yersinia enterocolitica*; confirm by Vitek or API).

Vibrio grows on thiosulphate citrate bile sucrose agar after 24 hours as ≥ 2mm colonies (*Vibrio cholerae* (sucrose fermenter): 2-3 mm yellow; *Vibrio parahaemolyticus* (lactose fermenter): 3-5 mm green). Fecal isolates are oxidase positive but this cannot be tested from thiosulphate citrate bile sucrose agar as false negatives occur. Full identification is made using the Vitek or API system and agglutination tests.

Colonies of *Clostridium difficile* on blood agar + cycloserine + cefoxitin agar after 48 hours of anaerobic incubation at 37°C are large, grey, irregular and have a distinctive putrid smell.

PRESUMPTIVE IDENTIFICATION OF URINE ISOLATES: One can also easily recognise the great majority of urinary isolates and identify them with well known, straightforward methods. 85% of urines with 10^5 organisms/mL produce recognisable growth after 4-6 hours incubation. The organisms can be presumptively identified with > 90% accuracy by a combination of colonial morphology, Gram stain and simple tests (eg., *Staphylococcus aureus* and coagulase negative staphylococci: slide coagulase or agglutination; *Proteus mirabilis*: non-lactose fermenting, oxidase and indole negative, urease positive; *Escherichia coli*: primary isolation plate colonial morphology + spot indole identifies 69% of isolates but spot indole can only be done from blood agar, fluorogenic β-glucuronidase assay identifies 87-94% in < 1 hour, usual method indole broth containing tryptophane (produces indole which reacts with p-dimethylaminobenzaldehyde, added after 2-4 hours incubation, to give a red colour.)

GROWTH CHARACTERISTICS ON CYSTINE LACTOSE ELECTROLYTE DEFICIENT MEDIUM AFTER 18 HOURS INCUBATION:

Escherichia coli: yellow, opaque colonies with a slightly deeper coloured centre, about 1.25 mm diameter (non-lactose fermenting strains: blue colonies)

Klebsiella: extremely mucoid colonies varying in colour from yellow to whitish blue

Proteus: translucent blue colonies usually smaller than *Escherichia coli*

Salmonella: flat blue colonies

Pseudomonas: green colonies with typical matt surface and rough periphery

Enterococcus faecalis: yellow opaque colonies about 0.5 mm diameter

Staphylococcus aureus: deep yellow colonies about 0.75 mm diameter, uniform in colour

Coagulase negative staphylococci: pale yellow or white, more opaque than *Enterococcus faecalis*, often with paler periphery

Corynebacterium: very small grey colonies

Lactobacillus: similar to *Corynebacterium* but with a rougher surface

Candida: small clear white to blue colonies

Streptococcus agalactiae: tiny clear blue colonies, often quite hard to see and easily missed after overnight incubation

IDENTIFICATION OF URINARY ISOLATES FROM CYSTINE LACTOSE ELECTROLYTE DEFICIENT AGAR:

A. Gram negative bacilli:

1. Smell, colonial appearance and oxidase reaction:

a. ? *Escherichia coli* (flat, non-mucoid lactose fermenting colonies): inoculate indole medium and read at 4-6 hours

indole positive = *Escherichia coli*

indole negative: inoculate MICROID, ATB32E, API20E or Vitek GNI

b. ? *Proteus*: inoculate urea broth, ornithine decarboxylase (inoculate one tube of ornithine decarboxylase medium and one of basal medium for each test; overlay each tube with paraffin so that it is anaerobic; if, after incubation, the basal medium is blue, the test is invalid), blood agar and indole and read at 4-6 hours

urea positive:

ODC positive (ODC tube blue, basal medium yellow), spreading on blood agar, indole negative = *Proteus mirabilis*

ODC positive, not spreading on blood agar, indole positive = *Morganella morganii*

ODC negative (ODC and basal medium tubes both yellow), spreading on blood agar, indole positive = *Proteus vulgaris*

ODC negative, not spreading on blood agar: inoculate API20E or Vitek GNI

c. ? *Pseudomonas*: perform oxidase test

oxidase positive: inoculate API20E + O-F glucose, nitrate, MacConkey and motility, or Vitek GNI

2. Other Gram negative bacilli: perform oxidase test and inoculate MICROID (oxidase negative only), ATB32E, API or Vitek GNI

B. Gram positive cocci: perform catalase test

1. Catalase positive = staphylococci and micrococci; perform Staphyslide test
   a. Staphyslide positive = *Staphylococcus aureus*
   b. Staphyslide negative: test novobiocin susceptibility and set up glucose O-F
      i. Novobiocin susceptible = coagulase negative staphylococcus other than *S.saprophyticus*
      ii. Novobiocin resistant, fermentative = *Staphylococcus saprophyticus*
      iii. Novobiocin resistant, oxidative = *Micrococcus*
2. Catalase negative: inoculate bile esculin, 6.5% NaCl, blood agar
   a. bile esculin positive, 6.5% NaCl positive = *Enterococcus*
   b. bile esculin positive, 6.5% NaCl negative = non-enterococcal group D *Streptococcus*
   c. bile esculin negative, 6.5% NaCl negative = other streptococci; use blood agar plate for grouping
   d. bile esculin negative, 6.5% NaCl positive = probably misidentified *Staphylococcus*; possibly *Aerococcus* (α-haemolytic on blood agar)

C. Yeasts: germ tube test verifies *Candida albicans* in 2-4 hours.

[**MICROID:** This system is intended to be used within the stipulated time span of 4-6 hours. This necessitates the use of a fairly heavy inoculum (usually several colonies), which in turn means that it should be used only where one is reasonably certain of being able to obtain an inoculum consisting entirely of one organism (especially since no purity check will be available when the strip is read). Be alert for insufficient inoculum density or incubation time. The majority of reactions should be clear-cut and sharp. Note particularly that *Escherichia coli* will give reactions of *Shigella* if insufficient reaction occurs. Always be suspicious of an identification (in any system) based only on a few characteristics. In the case of the MICROID, it is particularly important to check the oxidase reaction, especially where only nitrate and one or two other reactions are positive. If an unlikely identification or no identification occurs, check purity and set up an API20E or other system.]

IDENTIFICATION OF ISOLATES FROM GENITAL AND RESPIRATORY SPECIMENS is simplified by the facts that, as with feces, one is looking for a restricted range of pathogens and it is entirely possible to quickly become familiar with the appearance of both normal flora and pathogens from these sites on the various media employed (always look at the combination of media rather than making snap judgments based on the appearance on one). As long as one is alert to such rarities as *Haemophilus* in a urethral swab or *Pasteurella* in a sputum, the vast majority of isolates can be easily identified by the standard methods.

The simple scheme below will allow the identification of the great majority of isolates of **anaerobes**, at least to the degree required. *Bacteroides fragilis* may be identified rapidly by gas-liquid chromatography. The AnIdent and RapId ANA systems provide rapid identification of a variety of anaerobes, though with only $\approx$ 84% agreement with conventional systems.

A SIMPLE SCHEME FOR IDENTIFICATION OF ANAEROBES

Growth on BA + vitamin K, BA + vitamin K + vancomycin + kanamycin; no growth on CNA; metronidazole susceptible;

Gram stain $\rightarrow$ Gram negative bacilli

Vancomycin R kanamycin R colistin R(S)

Growth on bile esculin agar = *Bacteroides fragilis* group

No growth on bile esculin agar = *Bacteroides spp*

Vancomycin R kanamycin R colistin V, black pigment present = *Prevotella melaninogenica*

Vancomycin R kanamycin S colistin S

Pitting colonies

Urease positive = *Bacteroides ureolyticus*

Urease negative = *Campylobacter gracilis*

Colonies not pitting

Indole pos, growth on bile esculin pos, esculin neg, lipase neg = *Fusobacterium varium*

Indole positive, no growth on bile esculin, lipase pos = *Fusobacterium necrophorum*

Indole pos, no growth on bile esculin, lipase neg = *Fusobacterium nucleatum*
Indole neg, growth on bile esculin, esculin pos, lipase neg = *Fusobacterium mortiferum*

Growth on BA + vitamin K; no growth on BA + vitamin K + vancomycin + kanamycin, CNA; metronidazole susceptible; Gram stain → Gram negative cocci
Nitrate pos = *Veillonella*
Nitrate neg = *Acidaminococcus, Megasphaera*

Growth on BA + vitamin K, CNA; no growth on BA + vitamin K + vancomycin + kanamycin; metronidazole susceptibility variable; Gram stain → Gram positive cocci
SPS S = *Peptostreptococcus anaerobius*
SPS R
Indole pos = *Peptostreptococcus asaccharolyticus*
Indole neg = other *Peptostreptococcus spp*

Growth on BA + vitamin K, CNA; no growth on BA + vitamin K + vancomycin + kanamycin; metronidazole susceptibility variable; Gram stain → Gram positive bacilli
Diphtheroid-like
Catalase pos
Indole pos = *Propionibacterium*
Indole neg = *Rothia, Bifidobacterium*
Catalase neg = *Lactobacillus, Eubacterium*
Actinomyces-like → further testing
Clostridium-like
Double zone of hemolysis present, Nagler pos = *Clostridium perfringens*
Double zone of hemolysis absent
Heavy swarming
Spores terminal = *Clostridium tetani*
Spores subterminal = *Clostridium septicum*
Little or no swarming
Urease pos = *Clostridium sordellii*
Urease neg = other *Clostridium spp*

Most problems are likely to occur with aerobes isolated from specimens from sites other than those listed above. Even here, of course, the vast majority of isolates can be readily recognised by colonial appearance on the different media employed and identified in the usual simplistic manner.

Gram Negative Bacilli

Growth on MacConkey

Coliforms can usually be recognised by appearance and smell, and identified by GNI or API. Note that both systems have problems with *Enterobacter/Klebsiella*; in doubtful cases, a motility test may settle the question. Capsular swelling (the swelling of capsule on the surface of the bacterium in the presence of specific antiserum) may also be useful in identifying *Klebsiellla*.

Pseudomonas aeruginosa is usually recognisable by appearance (it commonly produces a green pigment) and distinctive odour. It is, of course, oxidase positive. It grows on blood agar, enriched chocolate agar with bacitracin and on MacConkey agar, but not on colistin nalidixic agar. It can, if necessary, be identified by GNI or API. [FN medium includes magnesium sulphate as activator of fluorescein production and nitrate to detect reduction of nitrate to nitrogen gas and helps differentiate *Pseudomonas* from other nonfermentative gram negative bacilli.]

Aeromonas can be recognised by its coliform appearance (it grows on MacConkey agar as a non-lactose fermenter, sometimes with a pink halo), β-hemolysis on blood agar, oxidase positivity and characteristic odour. It can be identified with GNI or API, though the GNI probably performs better overall. *Aeromonas* is always resistant to ampicillin.

One can also learn to recognise such organisms as *Flavobacterium*, *Burkholderia cepacia* and *Stenotrophomonas maltophilia* by appearance and smell.

Flavobacterium, *Alcaligenes* and *Achromobacter* are all oxidase positive organisms that are often resistant to aminoglycosides.

A Gram stain should be the first step for organisms whose probable identity is unknown. Curved rods are probably *Vibrio*. The GNI is now probably more reliable than the API for these organisms (the reverse of the previous case), but the identification may still need to be checked with such tests as growth on TCBS, O/129 susceptibility, salt tests, antibiotic susceptibilities (consult Balows).

Oxidase positive coccoid rods are probably *Moraxella*, which can possibly be identified with an NHI. In some cases, manual tests may be necessary.

Oxidase negative rods of similar morphology are probably *Acinetobacter*. This can be identified with the GNI, but with very few positive reactions; such a result should be checked by Gram stain if this has not already been done. Note that *Acinetobacter* is always resistant to penicillin.

For other isolates, perform oxidase and catalase tests and set up O-F, motility, urea and indole tests. Setting up a GNI or API may provide an identification, but this may well be incorrect. On the other hand, using the above few tests in Cowan and Steele's tables, Balow's keys and/or the Weaver-Hollis scheme will lead directly to an identification in many cases and provide a sure path to identification in most others.

No Growth on MacConkey, Growth on Blood Agar

The appearance and smell may well give a clue to the organism's identity. The Gram stain will also often be very helpful, being quite characteristic for many organisms in this group.

If you know the organism is an obligate aerobe, a combination of oxidase test, Gram stain and motility will soon tell you what genus you have. An oxidase negative organism will either be a *Pseudomonas* species or *Bordetella parapertussis*. These can be readily distinguished on Gram stain. An oxidase positive organism will either be *Pseudomonas*, *Flavobacterium*, *Bordetella parapertussis, Bordetella bronchiseptica* or *Moraxella*. The latter three organisms have quite characteristic Gram staining reactions. *Bordetella parapertussis* can be identified by serological reaction. *Bordetella bronchiseptica* gives a positive spot urease test in two minutes or a positive tube test in < 4 hours. *Moraxella* can be quite coccoid and may give a false negative string test. It can be loosely identified by NHI, more strictly by use of tables. *Pseudomonas* (motile) and *Flavobacterium* (nonmotile) can be separated on motility. They can be identified by GNI, though by no means all species are covered. Failing this, recourse must, if necessary, be made to one or other of the tables; the API is weak in this area.

If you know the organism is oxidative, the only choices are *Pseudomonas* and *Flavobacterium*.

Most people quickly learn to recognise *Pasteurella multocida* by sight and smell; it identifies well in the GNI and usually in the API, though addition of serum may be required.

Eikenella corrodens again is usually easily recognised by colonial appearance and smell, though it can be mistaken for a streptococcus. It can be identified in the API or NHI, but the easiest and most definitive identification is given by its unique requirement for X factor aerobically but not anaerobically.

Other organisms in this group for which Gram stain recognition is important are *Gardnerella*, *Brucella*, *Campylobacter* and salt-requiring *Vibrio* species. *Gardnerella* produces tiny non-hemolytic colonies resembling lactobacilli on blood agar but tiny β-hemolytic colonies on special *Gardnerella* medium. It is usually susceptible to metronidazole and always resistant to sulphonamides. *Vibrio* species can be identified by GNI or API, but the identification should be verified by other tests as given in Balows. Methods of identifying other organisms are well documented.

For other organisms which do not meet the above criteria, oxidase and catalase tests should be performed, O-F, indole, urea and nitrate tests set up and the appropriate keys and tables followed.

No Growth on Blood Agar, Growth on Enriched Chocolate Agar

Gram negative bacilli which may not grow on either MacConkey agar or blood agar but which grow on enriched chocolate agar are *Brucella*, *Campylobacter*, *Haemophilus* and *Streptobacillus moniliformis*. These can all be readily separated on cellular morphology and identified appropriately. *Haemophilus* is usually identified by its requirement for X and/or V factors. Water-soluble factors (X, V and X+V) are impregnated into discs or filter paper strips or rings and placed on a medium deficient in these factors (brain heart infusion or trypticase soy agar) which has been inoculated with the organism. Growth around a disc indicates a requirement. The porphyrin test is regarded as a more reliable test for X factor requirement than the X factor disc method. Organisms not requiring X factor convert δ-aminolevulinic acid to porphobilinogen, which is detected by fluorescence under UV or reaction with modified Ehrlich's reagent. A tube test for porphyrin production confirms *Haemophilus influenzae* in 4 hours. The Vitek NHI card correctly identifies 94% of *Haemophilus influenzae* and 96% of *Haemophilus parainfluenzae* isolates but only about half of the *Haemophilus* strains are correctly identified.

Gram Negative Cocci

Aerobic Gram negative cocci are *Neisseria* or *Moraxella* (*Branhamella)*. All species are strict aerobes and oxidase positive and have characteristic colonial and cellular morphology. *Neisseria gonorrhoeae*, *Neisseria meningitidis* and *Neisseria lactamica* are the only *Neisseria* species that regularly grow on New York City medium, while *Neisseria gonorrhoeae* and *Neisseria meningitidis* do not grow on nutrient agar. However, note that a high inoculum density can produce a false result in these tests and that nutrient agar means a nutrient agar such as brain heart infusion agar, not an enriched nutrient agar such as Columbia agar (on which *Neisseria meningitidis* will grow). *Neisseria* species can be identified by a rapid carbohydrate utilisation test in which balanced phosphate buffered saline containing phenol red indicator and drops (or discs) of carbohydrates is heavily inoculated and the reaction read at 4 hours; these tests are not, however, always completely reliable. The ONPG (o-nitrophenyl-β-galactopyranosidase) test detects delayed lactose fermenters by the production of yellow o-nitrophenol by β-galactosidase and is frequently preferred to lactose fermentation. Gonocheck 11 has 100% sensitivity and 99.6% specificity. The Phadebact Monoclonal GC test may be used to verify an isolate as *Neisseria gonorrhoeae* but the

reaction should be definitely positive and only in one of the two reagents. Used in this manner, it has a sensitivity of 97% and specificity of 100%. Otherwise, an NHI should be used, as it should be for other *Neisseria* species. The Vitek NHI card correctly identifies 100% of *N.cinerea*, 100% of *N.lactamica,* 99% of *N.gonorrhoeae* and 92% of *N.meningitidis*, but 0-9% of other *Neisseria* species and will not identify *Moraxella catarrhalis*. *Moraxella catarrhalis* is easily identified with the tributyrin test. Some strains of *Neisseria meningitidis* will not ferment carbohydrates on primary isolation but will often do so after a serious of rapid subcultures; these isolates can also be definitively be identified by PCR at a reference laboratory.

Gram Positive Cocci

The catalase test (5 seconds slide test) is, of course, the basic test for differentiating micrococci and staphylococci from streptococci. It is possible to get a false positive catalase test with *Enterococcus faecalis* taken from blood agar or enriched chocolate agar or with other streptococci by picking up blood cells with the colony from a blood agar plate. The fact that the organism dos not grow on mannitol salt agar will usually make this mistake apparent.

Micrococcus is fairly easily differentiated from *Staphylococcus* because it is strictly aerobic and oxidative, while *Staphylococcus* will grow anaerobically and is fermentative (glucose fermentation performed in yeast extract + 1% peptone). Cowan and Steele's table states that *Micrococcus* is oxidase positive. This is true, but only using a special procedure; using the normal method, it is negative.

Staphylococcus aureus grows on blood agar and colistin nalidixic acid agar and is catalase positive and coagulase positive. It is easily identified with Staphyslide. The negative control latex must always be used. If the negative control latex agglutinates, the test is invalid and a tube coagulase must be performed. False positives are very rare (make sure the organism is a *Staphylococcus*; organisms giving false positives include *Candida* and *Enterococcus faecalis*). False negatives are also uncommon but negative results should be checked with a tube coagulase if the colonial morphology or the clinical picture suggests a *Staphylococcus aureus*. There are reported instances of *Staphylococcus aureus* (usually associated with gentamicin treatment) which will not produce positive reactions in either of these tests or will do so only under such special circumstances as room temperature incubation or incubation in CO_2. These can be confirmed biochemically as *Staphylococcus aureus* using, eg, the API Staph. Unfortunately, the Vitek GPI depends on being told whether the isolate is coagulase positive or negative and is no help in these cases.

Coagulase negative staphylococci which are reported without further identification should be reported as such, not as *Staphylococcus epidermidis*. All reported isolates from blood cultures and hospital specimens should be identified using the GPI. There are some doubts about the absolute accuracy of some of these identifications, but at least it is more or less consistent and allows correlation between specimens and consequent information about possible sources of isolates from blood cultures.

Staphylococcus saprophyticus is readily differentiated from other staphylococci by novobiocin resistance. Some *Micrococcus* species are also novobiocin resistant; this rarely causes a problem but the two can be differentiated by anaerobic growth and O-F reaction if necessary. *Staphylococcus saprophyticus* regularly gives a positive reaction to both test and control ragents in the Staphyslide.

Rothia produces large, adherent colonies on blood agar, looks like a *Staphylococcus* in a Gram stain but is either catalase negative or weakly positive. Unlike micrococci and staphylococci, it will not grow in 6.5% NaCl.

The other catalase negative Gram positive cocci are *Enterococcus*, *Streptococcus*, *Lactococcus, Aerococcus, Gemella, Pediococcus* and *Leuconostoc*. *Enterococcus*, *Streptococcus*, *Lactococcus* and *Leuconostoc* all have similar morphology, though *Leuconostoc* tends to be coccobacillary. *Aerococcus, Gemella* and *Pediococcus* all have staphylococcal-like morphology. *Aerococcus* grows poorly anaerobically. *Enterococcus*, *Streptococcus*, *Lactococcus, Aerococcus* and *Gemella* can all be identified using the API Strep. A heavy suspension (MacFarlane #3) is made in 2-5 mL saline and the strip inoculated per instructions. A purity plate on blood agar is essential as a mixed inoculum makes any results invalid. An esculinase tube test verifies *Streptococcus pneumoniae* and group D streptococci in 30 minutes but bile solubility (tube method confirms *Streptococcus pneumoniae* in 5-15 minutes) and optochin tests are the most reliable for identification of *Streptococcus pneumoniae*. Capsular swelling (the swelling of capsule on the surface of the bacterium in the presence of specific antiserum) may also be useful. The bile-esculin test is used to differentiate group D streptococci from other streptococci, while the salt tolerance (6.5% sodium chloride) test is used in conjunction with the bile-esculin test to differentiate enterococci (*Enterococcus faecalis*, *E.faecium, E.durans*, *E.avium*) from non-enterococci (*Streptococcus equinus*). *Streptococcus pyogenes* is β-hemolytic on blood agar and colistin nalidixic acid agar and does not grow on MacConkey. A grouping is required for further identification. When used with isolation plates or broth cultures, Streptex is both sensitive and specific for grouping of β-haemolytic streptococci of groups A, B, C, F and G. However, use of grouping without other tests in speciation may give false results. Note especially that 'minute colony' strains of *Streptococcus anginosus* may group as A, C, F, G (or not at all); these should be clearly differentiated from 'classical' representatives of groups A, C and G. Note also that not all β-haemolytic colonies from throat swabs are streptococci; they may be *Haemophilus*, staphylococci, *Neisseria* and others. Further, Streptex and similar systems may give misleading results with α- or γ-hemolytic streptococci; in particular *Streptococcus pneumoniae* may group as group C. *Pediococcus* and *Leuconostoc* are both invariably resistant to vancomycin. It should, perhaps, be pointed out that the bile-esculin and 6.5% NaCl tests are by no means definitive for enterococci; most

lactococci, aerococci and *Leuconostoc*, and many pediococci, also give positive results for both tests. In addition, 95% of *Pediococcus* strains and 35% of *Leuconostoc* react with group D antiserum.

Gram Positive Bacilli

Perhaps the first thing that should be said is that the first stage table for Gram positive bacilli in Cowan and Steele contains a large number of errors of fact and should not be used.

Large, sporeforming, catalase positive, Gram positive bacilli are members of the genus *Bacillus.* They all grow aerobically and may or may not grow anaerobically. *Clostridium* is easily distinguished from *Bacillus* by being catalase negative and, except for *C.carnis, C.histolyticum* and *C.tertium*, by being strict anaerobes.

The problem in identifying *Bacillus* arises when such isolates are Gram negative, don't spore and are smaller than usual. The string test was actually developed to solve this problem but false positives do occur. However, unlike Gram negatives with which they could be confused, they are vancomycin susceptible. Procedures exist to induce sporing but these are somewhat cumbersome and don't always produce results. Identifying *Bacillus* species, when this is necessary, has been simplified by the advent of the Vitek *Bacillus* card.

Gram positive bacilli appearing in 48 hours or less are definitely not *Mycobacterium*, *Nocardia* or *Actinomyces*.

Slow-growing, fine, weakly Gram staining bacilli should be suspected of being *Mycobacterium* or *Nocardia* and a modified Ziehl-Neelsen stain performed. *Nocardia* will usually show some branching but a squash preparation may be necessary to show this, since it easily fragments. It may be difficult to demonstrate acid-fastness unless the isolate is growing on a high protein medium such as Lowenstein-Jensen or casein medium. *Actinomyces* may show somewhat similar morphology to *Mycobacterium* or *Nocardia* but grows anaerobically, whereas *Mycobacterium* and *Nocardia* are strict aerobes. So is *Streptomyces*, which, however, tends to have thicker filaments which show little fragmentation, and is never acid-fast. *Nocardia* has a very earthy odour, while the earthy odour of *Streptomyces* is almost overpowering. A number of other nocardiform species may be encountered, usually as environmental contaminants.

Dematophilus is another strict aerobe which consists of branching filaments. However, the rather bizarre appearance of the filaments, which branch at right angles, and the production of motile coccoid forms serve to distinguish it from the other organisms mentioned above.

Oerskovia also produces extensively branching filaments which break up into motile rods and coccoid elements. However, its appearance on Gram stain is quite dissimilar to *Dermatophilus* and it grows anaerobically. It is interesting in that it grows much better on blood agar than on enriched chocolate agar and is catalase positive when grown aerobically but negative when grown anaerobically.

As before, I am neglecting the strict anaerobes. Aerotolerant clostridia have already been mentioned. Of the other genera with aerotolerant species or strains, it can be said that, if catalase positive they will be *Propionibacterium*, while if catalase negative they will be *Actinomyces* or *Lactobacillus*. Colonial and cellular morphology should enable separation of the latter two genera. Lactobacilli can be mistaken for streptococci.

The non-acid-fast, non-sporing, regular, Gram positive rods include *Listeria* and *Erysipelothrix* as the most important genera. *Listeria* consists of small coccoid rods, is usually β-hemolytic, is catalase, esculin (an esculinase tube can be read after 30 minutes) and Voges-Proskauer [organism produces acetoin, which reacts with oxygen and 40% potassium hydroxide to produce diacetyl which produces a red colour with α-naphthol] positive and shows tumbling motility at 25°C; it can be identified with the GPI. *Erysipelothrix* is α-hemolytic, catalase negative and produces H_2S in triple sugar iron agar. It can be mistaken for a streptococcus. It can be identified in the GPI; unfortunately, while it seems to be always correctly identified with this system, other organisms, including streptococci, are sometimes identified as *Erysipelothrix*. Two other genera usually considered in this group are *Brochothrix* and *Kurthia*; these are of little, if any, clinical significance. *Brochothrix* is very similar to *Listeria* but is nonmotile and does not grow at 37°C. *Kurthia* is a strict aerobe, oxidase positive, esculin negative and glucose negative.

The corynebacteria and related coryneforms frequently cause problems. Any Gram positive rods which are not sporing, branching, filamentous or acid-fast, show some degree of pleomorphism and tend to stain irregularly are described as coryneform. This can include a lot of genera other than *Corynebacterium*, and many corynebacteria are quite regular both in cellular morphology and in Gram staining reaction. All one can do is to be sure that the organism is not an unusual representative of one of the other genera mentioned above and then attempt to identify it using the table in Balows, which includes all the species of *Corynebacterium* and related species of any medical relevance. If identification is not possible by this means, all that remains is usually to label it a 'diphtheroid'. This includes a large number of environmental and plant pathogen species of *Corynebacterium*, as well as such environmental and dairy genera as *Caseobacter, Aureobacterium, Microbacterium, Agromyces, Arthrobacter, Brevibacterium, Cellulomonas* and *Micromonospora. Arthrobacter* can be identified, with some difficulty, by its rod $\rightarrow$ cocci $\rightarrow$ rod cycle and other properties. Identification of the other genera usually requires such exotic methods as cell wall analysis, fatty acid analysis, G+C content of DNA, DNA-DNA hybridisation.

Conclusion

With the approach outlined above, the great majority of bacteria isolated in the clinical laboratory can be identified. This approach can be characterised as a systematic one guided by knowledge and verified by close attention to the properties of

the organism, with stress being placed on such basic properties as colonial and cellular morphology, smell, growth characteristics, possession of an oxidative or fermentative metabolism, oxidase and catalase reactions, and such other biochemical reactions as are known to be close to invariant for the organism. It is important not to be misled by a single anomalous test, whether this is due to poor technique, poor information or the nature of the organism. It is also necessary to realise the limits of one's expertise and when to yell for help.

Chapter 28

Antimicrobial Susceptibility Testing

The aim of the exercise is to find antibiotics which will be useful in eliminating an infection caused by an isolated organism in a given clinical situation. Selection of antibiotics, method of testing, and reporting of results are all important.

Methods of Choosing an Antibiotic

Empirical.

Depends on knowledge of likely pathogens and their probable susceptibilities.

May be applied:

Before, or without, culture.

Based on microscopy of a specimen.

Based on confirmed or presumptive identification of isolate.

Based on susceptibility testing.

Choice of an Antibiotic

Appropriate to organism.

Appropriate to clinical condition.

Appropriate to patient:

Age:

Neonate: chloramphenicol, sulphonamides, cotrimoxazole contraindicated.

Children: tetracyclines, quinolones contraindicated.

Elderly: cotrimoxazole, clindamycin contraindicated.

Pregnancy: see table below.

Breastfeeding: chloramphenicol, quinolones, sulphonamides, azithromycin, tetracyclines, cotrimoxazole contraindicated.

Genetic factors: sulphonamides in glucose-6-phosphate dehydrogenase deficient infants.

Interaction with other drugs:

Antibiotic potentiating or diminishing effect of other drug.

Other drug potentiating or diminishing effect of antibiotic.

Antibiotic increasing side-effect of other drug.

Other drug increasing side-effect of antibiotic.

Clinical condition of patient:

Renal failure: polymyxin B, nalidixic acid, sulphonamides, cotrimoxazole, tetracycline contraindicated.

Liver failure: sulphonamides, cotrimoxazole contraindicated.

Dialysis: nalidixic acid contraindicated.

Availability for treatment:

Hospital or outpatient.

Patient compliance.

Remote areas.

Government regulation.

Choosing Antibiotics to Test

Above considerations +:

Able to be tested by method used. Antibiotic may not be testable because:

Intrinsic qualities of antibiotic, eg, poor diffusibility, need for acidification to become active.

Not so far standardised or incapable of standardisation for method.

If it is known which antibiotic the patient is being, or will be, treated with, this should be tested if at all appropriate.

In mixed infections with multiple organisms, all possible efforts should be made to find a single antibiotic appropriate for treating all significant organisms.

ANTIBIOTIC USE IN PREGNANCY

Safe	Probably Safe	Safety Not Established	Likely to Cause Ill-Effects	Absolutely Contraindicated
Amoxycillin	Amoxycillin-clavulanate	Cefpirome	Capreomycin	
Ampicillin	Azithromycin	Ciprofloxacin	Clofazimine	
Benzathine penicillin	Aztreonam	Clarithromycin	Cotrimoxazole	
benzylpenicillin	Cefaclor	Colistin	Doxycycline	
Cephalexin	Cefepime	Cycloserine	Framycetin	
cephalothin	Cefotaxime	Dapsone	Sodium fusidate	
chloramphenicol	Cefotetan	Dicloxacillin	Gentamicin	
clindamycin	Cefoxitin	Enoxacin	Gramicidin	
cloxacillin	Cefpodoxime	Imipenem	Methacycline	
Erythromycin	Ceftazidime	Meropenem	Minocycline	
ethambutol	Ceftriaxone	Metronidazole	Neomycin	
hexamine	Cephamandole	Norfloxacin	Netilmicin	
Isoniazid	Cephazolin	Ofloxacin	Rifampicin	
lincomycin	Flucloxacillin	Teicoplanin	Silver sulphadiazine	
Nalidixic acid	Piperacillin	Ticarcillin	Streptomycin	
nitrofurantoin	Piperacillin-tazobactam	Ticarcillin-clavulanate	Sulphacetamide	
Phenoxymethyl penicillin	Roxithromycin	Trimethoprim	Sulphadiazine	
Procaine penicillin	Spectinomycin	Vancomycin	Sulphamethoxazole	
			Tetracycline	
			Tobramycin	

Testing

A successful outcome to therapy depends on the definition of a susceptible isolate as one where there has been a prior correlation with a favourable clinical response. All methods may give false susceptible results for some organisms showing intrinsic resistance, which may not be detected—eg, *Klebsiella* and ampicillin [see table of intrinsic resistances below]. Within limits, specificity is more important than sensitivity—ie, no false susceptibles, even at the expense of missing some that could be susceptible.

Intrinsic/Easily Induced Resistances

Organism	Report Resistant to
Acinetobacter	all cephalosporins
Enterobacter, Serratia, Citrobacter, Aeromonas, Providencia rettgeri, Providencia stuartii, Morganella morganii	ampicillin, cephalosporins, augmentin, ticarcillin
Proteus vulgaris, Proteus penneri	ampicillin, cephalosporins, ticarcillin, nitrofurantoin, tetracycline
Proteus mirabilis	tetracycline, nitrofurantoin, colistin
Klebsiella	ampicillin, ticarcillin
Yersinia enterocolitica	ampicillin
Pseudomonas aeruginosa	ampicillin, cephalothin, chloramphenicol, cotrimoxazole, tetracycline, augmentin
Stenotrophomonas maltophilia	ampicillin, augmentin, all cephalosporins, ciprofloxacin, norfloxacin, tetracycline, aminoglycosides

Methods

A standard method should be used.

Agar dilution is regarded as the 'gold standard', but results are influenced by agar, do not reflect high mutation rates, are somewhat time-consuming and prone to 'clerical' errors. Also, it is not applicable to bactericidal studies. Mast AdaTab system may be used to make accurate solutions; 'in house' solutions are less stable and more difficult to control.

The most suitable method overall appears to be broth microdilution (for both aerobes and anaerobes). It is a reference or standardised method which yields MICs directly over a wide range, does not require antimicrobial dilutions, has an alterable incubation routine, is uninfluenced by agar or diffusion rate, has divalent cation content controllable by performance testing or media supplementation, gives results which reflect high mutation rates by bacteria, is applicable to urgent direct susceptibility testing, is fairly easily individualised, and is applicable to bactericidal studies. Preparation of inocula directly from growth on agar plates gives as reproducible results as preliminary growth in broth. Commercially available products are convenient and accurate but relatively expensive and restricted to the range supplied by the manufacture. Of the commercial products available, Flow's MPS is the most accurate (95-97%) and reproducible (91-100%), while the Autobac MIC is the automated system with the best performance, giving 95% agreement with agar dilution. There are, however, problems in detecting methicillin resistance with these systems, the API Unispect KB being the only system giving results comparable with Kirby-Bauer. Broth dilution methods also have problems with sulphonamides, trimethoprim and aminoglycosides.

The Vitek semi-automated form of the broth microdilution method can produce results for Enterobacteriaceae in a minimum of 4 hours and for staphylococci in a minimum of 6 hours, allowing 70% of Vitek tests to be reported the same day. Because of this and because of its convenience when handling large numbers of isolates, it is widely used in larger laboratories. It is also the most accurate (specificity 93%) routine method for testing methicillin susceptibility, while also showing high sensitivity (96%). However, it has problems with testing ampicillin, cephalosporins and augmentin against Enterobacteriaceae, and all antibiotics against *Pseudomonas*. Also, the relatively large inoculum needed may result in false results due to mixed cultures, which may not be detected by the operator.

Problems with other automated systems include cephalothin against *Enterococcus*, aerobic Gram negative bacilli and MRSA, and kanamycin against *Pseudomonas aeruginosa* with Autobac 1; enterococcus with cephalothin, penicillin, gentamicin and kanamycin, *Enterobacter* with β-lactam drugs, and *Serratia* against colistin with MS-2.

The API - ATB uses a sloppy agar but is otherwise similar to manual broth microdilution methods.

Broth macrodilution methods are laborious, time-consuming and require careful technique. They have the disadvantages that antimicrobial dilutions are required, they are not applicable to urgent direct susceptibility testing, and are not easily individualised.

Agar diffusion is in many ways the least desirable. MICs are not directly obtainable, incubation routine is not alterable, it is influenced by agar and diffusion rate, results do not reflect high mutation rates by bacteria, and it is not applicable to bactericidal studies. However, no antimicrobial dilutions are required, it is applicable to urgent susceptibility testing, and antimicrobial tests are easily individualised. Because of this, agar diffusion methods are probably still the most widely used overall. They cannot be used for slow-growing organisms or for poorly diffusing antibiotics or for those whose activity depends on conditions which cannot be duplicated in the method.

Agar disc diffusion methods depend on finding break-points for each antibiotic by plotting MICs against zone size. A properly calibrated disc test is, in fact, a highly accurate, reproducible method of determining an MIC. If a susceptible isolate is defined as one where there has been a prior correlation with a favourable clinical response, the test predicts a successful outcome to antimicrobial therapy. If agar disc diffusion is used, a standard method such as Kirby-Bauer (NCCLS) or Bell's CDS method should be used.

The Kirby-Bauer (NCLS) method uses a single disc concentration for each antibiotic and finds the zone size corresponding to the MIC for susceptible organisms. Zone sizes may vary for different classes of organisms (eg, ampicillin with Enterobacteriaceae and with Staphylococci). If the category 'intermediate' is reported, this should indicate that the test result is equivocal. A more appropriate term is 'indeterminate', requiring an alternative test. A 'moderately susceptible' result should be reported to indicate susceptibility under certain conditions. Enterococci, other streptococci and non-penicillinase-producing, penicillin-susceptible organisms, when tested against penicillin or ampicillin, should be reported as 'moderately susceptible' rather than as 'intermediate'; this applies especially to enterococci, which for blood or serious invasive tissue infections require high dosage of penicillin or ampicillin, generally combined with an aminoglycoside for improved therapeutic response and bactericidal action. For streptococci, staphylococci and other penicillin-susceptible organisms, 'susceptible' means 'very susceptible'. When an intermediate result is obtained with staphylococci, the strains should be further investigated to determine if they are heteroresistant. The method is sensitive (> 96%) in testing for methicillin resistant staphylococci but its specificity is only 50%.

The CDS method attempts to find a disc concentration for each antibiotic which will give a susceptible zone size of ≥ 6 mm. Unfortunately, this is not always possible. It is easier to use than Kirby-Bauer and less prone to 'false susceptible' results but some antibiotics which can be tested by Kirby-Bauer cannot be by CDS. The method is only used in Australia and New Zealand.

The Stokes method compares zone sizes obtained for a test organism with those for a control organism. It is now rarely used in Australia because it is somewhat more troublesome to use and, in many cases, is less accurate than other disc diffusion methods. It does, however, show a specificity of 88% in testing staphylococci for methicillin resistance, while also having high sensitivity (> 96%)

The E-test uses a strip with a gradient of antibiotic. This allows the direct reading of the MIC (highly comparable to that obtained by dilution methods). The method is simple to use but expensive and is not useful for detecting extended broad spectrum beta-lactamase production.

Within limits, zone sizes in disc diffusion susceptibility testing are a function of inoculum density, lower densities producing larger zones. Depending on relative diffusion rates and stability characteristics of the antimicrobial and growth characteristics of the organism at room temperature and at incubation temperature, prediffusion prior to incubation may increase or decrease zone sizes; an increase is usual but by no means universal. In some cases, zone sizes may diminish with prolonged incubation, presumably because the drug has had a bacteriostatic effect and, with the passage of time, it has either leached out of the organism or has been metabolised, allowing the resumption of growth. Increased agar concentration decreases the diffusion rate of the drug and produces smaller zones. The depth of agar is also important, smaller volumes (< 17 mL for a 9 cm plate) giving larger zone sizes.

Antibiotic discs must be stored under the correct conditions. For β-lactams and some other antibiotics, this means in the freezer, not in the refrigerator.

Staphylococci must be incubated at 35°C, not at 37°C. Using a 0.5 U benzylpenicillin disc, susceptible strains of *Staphylococcus aureus* have a zone of inhibition of around 12 mm, while resistant strains have 0-1 mm zones. Rare strains with low penicillinase activity give zones of 4-5 mm with a sharp edge (MIC = 0.06 mg/L). *Staphylococcus saprophyticus* produces low levels of non-inducible penicillinase and gives zones of 5-7.5 mm with a 0.5U benzylpenicillin disc.

Resistance to methicillin is mainly due to the presence of altered PBP2a, which has poor affinity for methicillin and all other β-lactams, including imipenem and cephalothin. Therefore, resistance to methicillin implies resistance to all β-lactams. Only a minority of strains show 'homogenous' resistance, with all cells appearing to be resistant to high levels of methicillin. The majority of clinical isolates are thermosensitive heterogenous strains. These strains contain methicillin susceptible organisms that have the usual characteristics of nonheteroresistant *Staphylococcus aureus*, and methicillin resistant organisms which grow more slowly and may escape detection under ordinary conditions of culture and temperature. Only 1 in 10^4 to 1 in 10^7 organisms in such a population is resistant. Reducing the incubation temperature from 37°C to at least 35°C and increasing the osmolality of the culture medium by adding sodium chloride enhance expression of resistance to penicillinase-resistant penicillins in this subpopulation. Strains of *Staphylococcus aureus* have been described that require special culture conditions of temperature and osmolality but longer incubation periods (48 h) for expression of resistance to penicillinase resistant penicillins. These strains have been called acquired-resistant *Staphylococcus aureus*. They produce large quantities of β-lactamase and may be rendered susceptible by adding clavulanic acid. Some studies were unable to find clinical justification either for routine screening for acquired-resistant strains or for reporting these strains as methicillin resistant. Infections caused by acquired-resistant strains of *Staphylococcus aureus* appeared to respond well to therapy with the penicillinase-resistant penicillins and at least as well as to therapy with other agents, including vancomycin. The solution may be to regard only amoxycillin-clavulanate resistant isolates as showing resistance to penicillinase-resistant penicillins.

Heterogenous strains of coagulase negative staphylococci also occur but these do not show resistance at 30°C nor on mannitol salt agar at 35°C. The CDS method is not reliable for testing.

Definitive testing for methicillin resistance can be performed using PCR or the Mastalex kit for detection of PBP2a.

If a tetrazolium dye is incorporated into the medium, results can be read in 1-3 hours, with identical results to standard methods.

In general, susceptibility tests should be performed on media as minimal as is required for growth. The zone sizes obtained with aminoglycosides, particularly when testing *Pseudomonas aeruginosa*, are very medium dependent because of variations in divalent cation content. With *Pseudomonas* species tested against aminoglycosides, the degree of susceptibility obtained varies inversely with the concentration of calcium and magnesium ions in the medium. Organisms in the intermediate category may be either susceptible or resistant when tested by dilution methods and should therefore more properly be classified as 'indeterminant'. A number of media have been specially formulated for susceptibility testing. In most applications, they are quite comparable, though some may be found incapable of supporting the growth of some organisms which will grow well on others. With organisms requiring blood or serum for growth, normal susceptibility medium + lysed blood should be used, the lysing process inactivating sulphonamide inhibitors present in whole blood. Media used for sulphonamide and trimethoprim testing should also be as thymidine free as possible. For those organisms requiring chocolated blood, susceptibility tests may be carried out using such media, but in such a case, sulphonamides and trimethoprim should be reported as susceptible if any diminution of growth in the vicinity of the disc is observed. Generally, however, Muller-Hinton or similar agar supplemented with 5% lysed horse blood and 1% IsoVitalex or comparable supplement and adjusted to pH 7.2 should be used. Susceptibility tests should not be performed on media containing antibiotics.

Cases most likely to yield unacceptable results by whichever method is used include *Enterobacter* testing with cefamandole, where discrepant (usually false susceptible) results are generally due to mutant resistant subpopulations or depressed β-lactamase activity requiring induction or other technical modifications, and the clinically irrelevant ampicillin and cephalothin; *Proteus/Providencia* testing against clinically irrelevant nitrofurantoin; *Serratia* testing against clinically

irrelevant polymyxins; *Pseudomonas aeruginosa* testing against gentamicin and the clinically irrelevant kanamycin and chloramphenicol; enterococci against erythromycin and the clinically irrelevant cephalothin, clindamycin and aminoglycosides; *Staphylococcus aureus* against erythromycin and methicillin; coagulase negative staphylococci against penicillin and tetracycline.

The correlation of cephalothin MIC with the zone size using a disc diffusion test gives a continuous distribution of susceptibility and, therefore, cephalothin cannot be used for disc testing. Susceptibility of *Staphylococcus aureus* to cephalothin can be inferred from susceptibility to methicillin. Susceptibility of Enterobacteriaceae (except those which produce a Class I chromosomal β-lactamase) to cephalothin can be inferred from susceptibility to ampicillin.

The following antimicrobials should be tested (others whose susceptibility/resistance can be inferred from those tested shown in brackets; see also tables below):

Staphylococci: benzylpenicillin (phenoxymethylpenicillin, phenethicillin, amoxycillin, ampicillin and analogues, azlocillin, carbenicillin, mezlocillin, piperacillin, ticarcillin; in CDS, test and report ampicillin (extrapolate benzylpenicillin, amoxycillin and cephalothin) for *S.saprophyticus*), methicillin (CDS; cannot test *S.saprophyticus*—always report sensitive) or oxacillin (NCCLS) (amoxycillin-clavulanate, cephalosporins (staphylococci exhibiting resistance must be reported resistant to all cephalosporins, because in most cases they are clinically ineffective), cloxacillin, dicloxacillin, flucloxacillin, oxacillin, ticarcillin-clavulanate), cephalexin (CDS *S.saprophyticus* in urines only), erythromycin (clindamycin, lincomycin; do not report for urinary or blood culture isolates), tetracycline (all tetracyclines; do not report for urinary or blood isolates); cotrimoxazole or trimethoprim (test and report for urinary isolates only; in CDS, sulphafurazole and trimethoprim are tested separately), vancomycin (MRSA and coagulase negative staphylococci from sterile sites only), rifampicin (MRSA only), fusidic acid (MRSA only), ciprofloxacin (MRSA and urine isolates only; report as norfloxacin in urinary isolates), nitrofurantoin (urine isolates only), chloramphenicol (isolates from eye infections only)

Enterococci: no cephalosporins (always report as resistant); ampicillin (amoxycillin, ampicillin analogues, apalcillin, azlocillin, mezlocillin, benzylpenicillin, piperacillin), cotrimoxazole or trimethoprim (NCCLS only), vancomycin (report if allergic to penicillin, resistant to ampicillin or if from peritoneal dialysates or other sterile sites), gentamicin (high level resistance in blood culture isolates only; NCCLS: brain heart infusion agar plate with 500 μg/mL gentamicin or 120 μg disc of gentamicin; CDS: use 200 μg disc), nitrofurantoin (urinary isolates only)

Streptococci: incubate *Streptococcus pneumoniae* and *Streptococcus milleri* in 5% CO_2; penicillin (NCCLS agar dilution and automated, CDS) or oxacillin (NCCLS disc methods to test pneumococci for relative resistance to penicillin) (penicillin (all relatively resistant pneumococci should have MIC determined, eg., by, E test), ampicillin and amoxycillin (report only if also reporting *Haemophilus influenzae*), ticarcillin, piperacillin, azlocillin, cephalothin and cephalexin (if MIC > 0.06 mg/L, report as resistant)), erythromycin (not CSF or urine), tetracycline (doxycycline, minocycline; *Streptococcus pneumoniae* respiratory or blood), cotrimoxazole or trimethoprim (NCCLS: only report on resistant pneumococci; CDS: Group B streptococci from urine only), chloramphenicol (resistant *Streptococcus pneumoniae* and eye isolates only), cefotaxime or ceftriaxone (NCCLS: test and report for CSF and blood isolates only; CDS: test and report for resistant *S.pneumoniae* only), vancomycin (if allergic to penicillin or for blood cultures, serious nosocomial infections or resistant strains), nitrofurantoin (CDS urinary only)

Enterobacteriaceae and Other Gram Negative Rods: ampicillin (amoxycillin; *Enterobacter, Serratia, Citrobacter freundii, Acinetobacter, Proteus vulgaris, Proteus penneri, Providencia, Morganella morganii* either report all isolates resistant regardless of result or, if susceptible, issue actual result with comment such as 'may result in selection of resistance during therapy'; all isolates of *Aeromonas* should be reported as resistant to all penicillins), amoxycillin-clavulanate (report if β-lactamase producer; report result for organisms listed under ampicillin similarly as for ampicillin), cephalothin (NCCLS only; CDS: extrapolate from ampicillin) and cephalexin (CDS: urinary isolates only; report result for organisms listed under ampicillin similarly as for ampicillin), cefotaxime (ceftriaxone, cefmenoxime, ceftazidime, ceftizoxime, moxalactam; report result for organisms listed under ampicillin similarly as for ampicillin; do not report for urinary isolates unless resistant to amoxycillin, amoxycillin-clavulanate and cephalexin; strains of *Aeromonas* demonstrating presence of inducible cephalosporinase by flattening of inhibitory zone around a cefotaxime 5 μg disc adjacent to an imipenem 10 μg disc or showing resistant mutants which appear as colonies within the zone of inhibition around disc containing any cephalosporin, cephamycin or aztreonam should be regarded as resistant to aztreonam, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftriaxone and cephalexin), cotrimoxazole or trimethoprim (CDS: sulphafurazole and trimethoprim are tested separately), gentamicin, amikacin (test only if resistant to gentamicin, report only if resistant to other aminoglycosides), norfloxacin (test for urinary isolates only, report only for organisms listed under ampicillin or multi-resistant urinary isolates), ciprofloxacin (report for organisms listed under ampicillin and multi-resistant non-urinary isolates), nitrofurantoin (test and report for urinary isolates only; report resistant for *Proteus, Morganella morganii, Providencia, Serratia*), tetracycline (not urinary isolates or faecal isolates other than *Vibrio*), ticarcillin (multi-resistant organisms, hospital patients or on request only), tobramycin (multi-resistant organisms, hospital patients or on request only), ceftazidime (multi-resistant organisms, hospital patients or on request only); strains of *Aeromonas* which produce mutant colonies within the zone of inhibition should be regarded as resistant to imipenem irrespective of size of inhibitory zone

Pseudomonas aeruginosa and ***Burkholderia***: ceftazidime (cefperazone, cefsulodin; isolates from blood cultures, cystic fibrosis patients or on request only), ticarcillin or piperacillin (apalcillin, azlocillin, mezlocillin), gentamicin, tobramycin (report only if resistant to gentamicin), amikacin (test and report only if resistant to other aminoglycosides) ciprofloxacin (do not report for urinary isolates unless resistant to norfloxacin or on request), norfloxacin (urinary isolates only), imipenem (on request only), polymyxin B (colistin; isolates from external ear infections only)

Haemophilus influenzae, Moraxella catarrhalis: benzylpenicillin (CDS: test for *M.catarrhalis* only; do not report, but extrapolate ampicillin/amoxycillin result; possibly all resistant in clinical practice), ampicillin (amoxycillin, i.v. benzylpenicillin; CDS: *H.influenzae* only (check all susceptible isolate for beta-lactamase production and report resistant if positive), extrapolate from penicillin result for *M.catarrhalis*), cefaclor (CDS: *H.influenzae* only non-encapsulated strains), amoxycillin-clavulanate (NCCLS: dilution methods only; CDS: *Haemophilus influenzae* only for non-encapsulated strains, report if a β-lactamase producer), cefpodoxime (CDS *M.catarrhalis* only; do not report), cefotaxime (ceftriaxone, ceftazidime; *H.influenzae* only; report if a β-lactamase producer and invasive isolate; CDS: extrapolate from cefpodoxime for *M.catarrhalis*), tetracycline (NCCLS; CDS: *H.influenzae* non-encapsulated strains only), cotrimoxazole, chloramphenicol (invasive *Haemophilus* only; may be better to test for chloramphenicol acetyl transferase, using a commercial enzyme detection kit or by the 'clover leaf' method), rifampicin (NCCLS only; test and report for invasive *Haemophilus*), erythromycin (test and report only for *M.catarrhalis*), β-lactamase test

Stenotrophomonas maltophilia: may appear susceptible to antimicrobials on in vitro testing to which it has a high rate of mutation to resistance (cotrimoxazole is considered the antimicrobial of choice); ticarcillin-clavulanate, piperacillin-tazobactam, ceftazidime, imipenem, gentamicin, tobramycin and cotrimoxazole are tested in NCCLS, though the clinical efficacy of ticarcillin-clavulanate and piperacillin-tazobactam is uncertain and imipenem, gentamicin and tobramycin are always reported as resistant; in CDS, sulphafurazole is tested and reported

Listeria monocytogenes: penicillin (for CDS, extrapolate from ampicillin), erythromycin (NCCLS only), ampicillin (amoxycillin), no cephalosporins (report resistant), gentamicin, chloramphenicol (NCCLS only; report only for CSF isolates), vancomycin (NCCLS only; report if resistant to penicillin or if peritoneal dialysate isolate)

Neisseria meningitidis: penicillin, chloramphenicol, cefotaxime or ceftriaxone, rifampicin (NCCLS only; report only if testing and only if resistant), ciprofloxacin (NCCLS only; report only if testing and only if resistant)

Neisseria gonorrhoeae: β-lactamase test; penicillin, ceftriaxone, spectinomycin, tetracycline (not testable by disc diffusion methods)

Guidelines for Antibiotic Susceptibility Testing and Reporting Using CDS System

Staphylococcus (Sensitest, air, 35°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
benzylpenicillin[1]	0.5 U	penicillin, ampicillin, amoxycillin		≤ 0.06 mg/L
methicillin[1]	5 μg	dicloxacillin, flucloxacillin, cephalosporins[2]	augmentin, cloxacillin	≤ 4 mg/L
erythromycin[3]	5 μg	erythromycin	azithromycin, roxithromycin, lincomycin, clindamycin	≤ 0.5 mg/L
tetracycline[3]	30 μg	tetracycline	all tetracyclines	≤ 4 mg/L
ciprofloxacin[4,5]	2.5 μg	norfloxacin		≤ 1 mg/L
sulphafurazole	300 μg	cotrimoxazole[6]		≤ 64 mg/L
trimethoprim[5]	5 μg	trimethoprim, cotrimoxazole[6]		≤ 2 mg/L
nitrofurantoin[5]	200 μg	nitrofurantoin		≤ 32 mg/L
vancomycin[7,8]	5 μg	vancomycin		≤ 4 mg/L
rifampicin[7]	1μg	rifampicin		≤ 0.5 mg/L
fusidic acid[7]	2.5 μg	fusidic acid		≤ 0.5 mg/L
Chloramphenicol[8,9]	30μg	chloramphenicol		≤ 8 mg/L
ampicillin[4]	5 μg	penicillin, ampicillin, amoxycillin		≤ 0.5 mg/L
cephalexin[4]	100 μg	cephalexin		≤ 16 mg/L
gentamicin	10 μg	gentamicin		≤ 1 mg/L
kanamycin	50 μg	kanamycin		≤ 8 mg/L
teicoplanin	15 μg	teicoplanin		≤ 8 mg/L

Notes:

1. Not *S.saprophyticus.*
2. Ceftazidime is considered inactive.
3. Not for blood or urinary isolates.
4. *S.saprophyticus* only.
5. Urine isolates only.
6. Report as susceptible to cotrimoxazole unless resistant to both sulphafurazole and trimethoprim.
7. Methicillin resistant *S.aureus* only.
8. Zone size for susceptible isolates = 2 mm.
9. Isolates from eye infections only.

Streptococcus (Blood Sensitest, air[1], 35 °C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
benzylpenicillin[2]	0.5 U	penicillin, ampicillin, amoxycillin	cephalosporins[3]	≤ 0.25 mg/L
ampicillin	5 μg	see note 2		≤ 2 mg/L
erythromycin[4]	5 μg	erythromycin	azithromycin, roxithromycin, lincomycin, clindamycin	≤ 0.5 mg/L
tetracycline[4]	30 μg	tetracycline	all tetracyclines	≤ 4 mg/l
nitrofurantoin[5]	200 μg	nitrofurantoin		≤ 32 mg/L
vancomycin[6,7]	5 μg	vancomycin		≤ 4 mg/L
ceftriaxone[8]	5 μg	ceftriaxone		≤ 2 mg/L
chloramphenicol[7,9]	30 μg	chloramphenicol		≤ 8 mg/L
cotrimoxazole[10]	25 μg	cotrimoxazole		≤ 0.5/9.5 mg/L

Notes:

1. Incubate *S.pneumoniae* and *S.milleri* in 5% CO_2.
2. If resistant and isolate not from CSF, test ampicillin and, if susceptible, report 'isolate shows reduced susceptibility to penicillin but may, in clinical practice, respond to higher doses of penicillin, ampicillin or amoxycillin'.
3. Groups A, B, C, F and G only. Ceftazidime is considered inactive against Gram positive organisms.
4. Not CSF or urinary isolates.
5. Urinary isolates only.
6. If allergic to penicillin or for blood cultures, serious nosocomial infections or resistant strains.
7. Zone size for susceptible isolates = 2 mm.
8. Resistant *S.pneumoniae* isolates only.
9. Resistant *S.pneumoniae* isolates and isolates from eye infections only.
10. *Streptococcus pneumoniae* and Group B streptococci only.

Enterococci (Blood Sensitest, air, 35°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
nitrofurantoin[1]	200 μg	nitrofurantoin		≤ 64 mg/L
vancomycin[2,3]	5 μg	vancomycin		≤ 4 mg/L
ampicillin[4]	5 μg	benzylpenicillin, ampicillin, amoxycillin		≤ 2 mg/L
gentamicin[5]	200 μg	see note 6		≤ 512 mg/L

Notes:

1. Urinary isolates only.
2. If allergic to penicillin, resistant to ampicillin or from sterile sites.
3. Zone size for susceptible isolates ≥ 2 mm. Hazy zone edge indicates possible low level resistance (VanB type) even if zone size > 2 mm.
4. Zone < 4 mm = resistant. Perform a cefinase test for β-lactamase on strains with an annular radius of 4-6 mm. β-lactamase positive strains are reported as resistant. β-lactamase negative strains are reported as 'reduced susceptibility to ampicillin'.
5. Blood culture isolates only. Zone size for susceptible isolates ≥ 4 mm.
6. Report susceptible/resistant as 'no/high level resistance to gentamicin, which may affect synergy with penicillins, demonstrated'.

Enterobacteriaceae, Vibrionaceae and *Acinetobacter* (Sensitest, air, 35°C)[1,2,3]

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
tetracycline[4]	30 μg	tetracycline	all tetracyclines	≤ 4 mg/L
ciprofloxacin[5]	2.5 μg	ciprofloxacin		≤ 1 mg/l
sulphafurazole	300 μg	cotrimoxazole[6]		≤ 64 mg/L
trimethoprim	5 μg	trimethoprim (urines only) cotrimoxazole[6]		≤ 2 mg/L
nitrofurantoin[7]	200 μg	nitrofurantoin		≤ 32 mg/L
norfloxacin[7]	10 μg	norfloxacin		≤ 4 mg/L
gentamicin	10 μg	gentamicin		≤ 1 mg/L
cephalexin	100 μg	cephalexin		≤ 16 mg/L
ampicillin	25 μg	ampicillin, amoxycillin	cephalothin[8], piperacillin, ticarcillin	≤ 8 mg/L
augmentin	60 μg	augmentin[9]		< 16/8 mg/L
tobramycin[5]	10 μg	tobramycin		< 1 mg/L
ceftazidime[5]	10 μg	ceftazidime		≤ 4 mg/L
cefotaxime[5]	5 μg	cefotaxime		≤ 1 mg/L
amikacin[5]	30 μg	amikacin		≤ 4 mg/L
aztreonam[5]	30 μg	aztreonam		≤ 8 mg/L
cefipime[5]	10 μg	cefipime		≤ 1 mg/L
cefotetan[5]	30 μg	cefotetan		≤ 8 mg/L
cefoxitin[5]	30 μg	cefoxitin		≤ 8 mg/L
cefpirome[5]	10 μg	cefpirome		≤ 2 mg/L
cefpodoxime[5]	10 μg	cefpodoxime		≤ 2 mg/l
ceftriaxone[5]	5 μg	ceftriaxone		≤ 1 mg/L
cephazolin[5]	30 μg	cephazolin		≤ 16 mg/L
chloramphenicol	30 μg	chloramphenicol		≤ 8 mg/L
enoxacin	10 μg	enoxacin		≤ 4 mg/L
imipenem[5]	10 μg	imipenem		≤ 4 mg/L
kanamycin	50 μg	kanamycin		≤ 8 mg/L
meropenem	5 μg	meropenem		≤ 2 mg/L
nalidixic acid[7]	30 μg	nalidixic acid		≤ 4 mg/L
netilmicin[5]	30 μg	netilmicin		≤ 2 mg/L
tazocin	55 μg	tazocin[10]		≤ 16/2 mg/L
timentim	85 μg	timentim[10]		≤ 32/2 mg/L

Notes:

1. Certain organisms exhibit intrinsic resistance or easily inducible resistance to certain organisms, that may not be detected on disc testing. In such cases, the organisms involved should always be reported as resistant regardless of the result of disc testing. The relevant organism/antibiotic combinations are listed in the table of **Intrinsic/Easily Induced Resistances** earlier in the chapter.
2. Multi-resistant isolates (especially *Klebsiella*) should be tested for extended broad spectrum beta-lactamase production by Casal's 'keyhole' method.
3. *Yersinia enterocolitica* is incubated in air at 30°C.
4. Not urinary isolates or faecal isolates other than *Vibrio*.
5. Multi-resistant organisms, hospital patients or on request only.
6. Report as susceptible to cotrimoxazole unless resistant to both sulphafurazole and trimethoprim.
7. Urinary isolates only.
8. Not for *Acinetobacter.*
9. If ampicillin resistant. If an ESBL is present, report for isolates from urine only.
10. If an ESBL is present, report resistant.

Listeria monocytogenes (Blood Sensitest, air, 35°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
ampicillin	5 μg	benzylpenicillin, ampicillin, amoxycillin		≤ 1 mg/L
gentamicin	10 μg	gentamicin		≤ 1 mg/L

Pseudomonas, Burkholderia (Sensitest, air, 35°C)[1]

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
ciprofloxacin[2]	2.5μg	ciprofloxacin		≤ 1 mg/L
norfloxacin[3]	10μg	norfloxacin		≤ 4 mg/L
gentamicin[4]	10μg	gentamicin		≤ 4 mg/L
ticarcillin	75μg	ticarcillin		≤ 32 mg/L
tobramycin[4]	10μg	tobramycin		≤ 4 mg/L
ceftazidime[5]	10μg	ceftazidime		≤ 4 mg/L
imipenem[6]	10μg	imipenem		≤ 4 mg/L
polymyxyin b[4,7]	300U	colistin, polymyxin B		≤ 1 mg/L
amikacin[6]	30 μg	amikacin		≤ 16 mg/L
aztreonam[6]	30 μg	aztreonam		≤ 8 mg/L
cefipime[6]	10 μg	cefipime		≤ 2 mg/L
cefpirome[6]	10 μg	cefpirome		≤ 2 mg/L
meropenem[6]	5 μg	meropenem		≤ 2 mg/L
netilmicin[4,6]	30 μg	netilmicin		≤ 8 mg/L
piperacillin[6]	50 μg	piperacillin		≤ 16 mg/L
sulphafurazole[8]	300 μg	cotrimoxazole		≤ 64 mg/L
trimethoprim[8]	5 μg	trimethoprim (urines only), cotrimoxazole[9]		≤ 2 mg/L
tazocin[6]	55 μg	tazocin		≤ 16/2 mg/L
timentim	5 μg	timentim		≤ 32/2 mg/L

Notes:

1. Regardless of results on disc testing, these organisms should be considered resistant to all other antibiotics listed under 'Enterobacteriaceae, Vibrionaceae and Acinetobacter'.
2. Not urinary isolates unless resistant to norfloxacin or on request.
3. Urinary isolates only.
4. Zone size for susceptible isolates ≥ 4 mm.
5. Isolates from blood cultures, cystic fibrosis patients or on request only.
6. On request only.
7. Isolates from external ear infections only.
8. Not *Pseudomonas aeruginosa*.
9. Report as susceptible to cotrimoxazole unless resistant to both sulphafurazole and trimethoprim.

Stenotrophomonas maltophilia

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred
sulphafurazole	300 μg	cotrimoxazole	

Haemophilus (HTM agar, CO_2, 35°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
ampicillin[1]	5 μg	ampicillin, amoxycillin		≤1 mg/L
cefotaxime[2]	0.5 μg	cefotaxime, ceftriaxone	ceftazidime	≤ 0.25 mg/L
ceftriaxone[2]	0.5 μg	cefotaxime, ceftriaxone	ceftazidime	≤ 0.25 mg/L
tetracycline	30μg	tetracycline	all tetracyclines	≤ 4 mg/L
cotrimoxazole	25μg	cotrimoxazole		≤ 1/19 mg/l
cefaclor	30μg	cefaclor		≤ 4 mg/L
augmentin[3]	15μg	augmentin		≤ 2 mg/L
chloramphenicol[4]	10μg	chloramphenicol		≤ 2 mg/L
cefpodoxime	10 μg	cefpodoxime		≤ 2 mg/l
ciprofloxacin	2.5 μg	ciprofloxacin		≤ 1 mg/L

Notes:

1. Check all isolates susceptible by CDS for beta-lactamase production and report resistant if positive.
2. Isolates from CSF and other serious infections only.
3. If beta-lactamase positive.
4. Isolates from CSF, serious systemic infections or eye infections only.

Moraxella catarrhalis (Blood Sensitest, O_2, 35°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
benzylpenicillin[1]	0.5 U	penicillin, ampicillin, amoxycillin		≤ 0.25 mg/L
erythromycin	5 μg	erythromycin	azithromycin, roxithromycin,	≤ 0.5 mg/L
tetracycline	30 μg	tetracycline	all tetracyclines	≤ 4 mg/L
cotrimoxazole	25 μg	cotrimoxazole		≤ 1/19 mg/L
cefaclor	30 μg	cefaclor, augmentin		≤ 4 mg/L
cefpodoxime	10 μg	cefpodoxime		≤ 2 mg/l
ciprofloxacin	2.5 μg	ciprofloxacin		≤ 1 mg/L

Notes:

1. Probably all resistant in clinical practice.

Campylobacter (Blood Sensitest, microaerophilic, 42°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
Erythromycin[1]	5 μg	Erythromycin	Azithromycin, roxithromycin,	≤ 0.5 mg/L
Tetracycline	30 μg	Tetracycline	All tetracyclines	≤ 4 mg/L
Ciprofloxacin	2.5 μg	Ciprofloxacin		≤ 1 mg/L
Gentamicin	10 μg	Gentamicin		≤ 1 mg/L

Notes:

1. Zone size for susceptible isolates ≥ 4 mm.

Neisseria meningitidis (Blood Sensitest, CO_2, 35°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
Benzylpenicillin	0.5 U	Penicillin	Ampicillin, amoxycillin	≤ 0.25 mg/L
Cefotaxime	0.5 μg	Cefotaxime		≤ 0.25 mg/L
Ceftriaxone	0.5 μg	Ceftriaxone		≤ 0.25 mg/L
Chloramphenicol	10 μg	Chloramphenicol		≤ 2 mg/L
Ciprofloxacin	2.5 μg	Ciprofloxacin		≤ 1 mg/L
Rifampicin	1 μg	Rifampicin		≤ 0.5 mg/l

Pasteurella multocida (Sensitest, air, 35°C)

Disc Tested	Potency	Antibiotics Reported	Other Antibiotics Whose Susceptibility/Resistance May Be Inferred	MIC for Susceptible Strains
Ampicillin	5 μg	Penicillin, ampicillin, amoxycillin		≤ 1 mg/L
Ciprofloxacin	2.5 μg	Ciprofloxacin		≤ 1 mg/L
Tetracycline	30 μg	Tetracycline	All tetracyclines	≤ 4 mg/L

Note that, while tetracycline is used as the class disc for all tetracyclines, certain organisms may be more susceptible to doxycycline and/or minocycline than to tetracycline.

CDS Susceptibility Method: Use only approved media. Plates should be dried before use. Using standard nichrome wire, touch the tops of 2 colonies and transfer to 5 mL sterile saline. Flood the plate with the suspension, making sure the surface is covered. Tilt the plate and remove the excess suspension with a pipette. Invert the plate and allow to dry at room temperature with the lid partially removed for 45 minutes. Place no more than 6 discs on each plate. Incubate at 35°C for approximately 18 hours in air (except *Haemophilus, Streptococcus milleri* and *Streptococcus pneumoniae,* which are incubated in CO_2).

Points to Watch in Using CDS

The method must be followed precisely.
The inoculum density is important; a higher density → smaller zones, lower density → larger zones.
Using the wrong medium, or the wrong atmosphere, for an organism can completely invalidate the result.
A wet surface when discs are placed on the plate may affect zone size or make zone sizes unreadable.
Prediffusion prior to incubation usually gives increased zones.
Prolonged incubation may give decreased zones.

Reporting

Class Agents: either report the class agent if this is clearly understood by medicos to include all members of the class (eg, tetracycline) or the most appropriate member if the connection is less obvious or the patient is known to be treated with a particular antibiotic.
Surrogate Agents: remember that some antibiotics stand in for others; eg, cephalothin cannot be tested by CDS but susceptibility to cephalothin can be inferred from the result for methicillin for Staphylococci and from ampicillin for Enterobacteriaceae.
Remember intrinsic resistances.
Remember contraindications.

Antibiotic Therapy for Anaerobes

No satisfactory, standardised methods exist for determination of the susceptibility of anaerobic isolates to antibiotics. Penicillin is the treatment of choice for all Gram positive anaerobes except *Clostridium difficile*, for anaerobic Gram negative cocci, and for beta-lactamase negative anaerobic Gram negative bacilli. Metronidazole is the treatment of choice for *Clostridium difficile*, for beta-lactamase positive anaerobic Gram negative bacilli and for most other anaerobes where patient penicillin hypersensitivity is a problem (erythromycin may be more useful for anaerobic Gram positive cocci). Most anaerobes are susceptible to clindamycin and chloramphenicol, but these will rarely be used unless the other choices are completely inappropriate. In situations of mixed aerobic and anaerobic infections, particularly those involving aerobic

Gram negative bacilli, augmentin or timentim may be appropriate. The broth-disc technique may be used for antibiotic susceptibility tests on anaerobes, but tetracycline, and perhaps erythromycin, yield discrepant results.

Beta-lactamase: With organisms where β-lactamase production is the sole, or main, method of resistance to β-lactams, β-lactamase testing may substitute for disc testing. This is particularly important for *N.gonorrhoeae* and *Bacteroides*, which cannot be tested by disc methods. Staphylococci and *Haemophilus* may show susceptible zones for β-lactams on disc testing but produce β-lactamase which can inactivate these antibiotics. The apparent susceptibility of these isolates must, therefore, be checked by β-lactamase testing. The acidimetric paper strip or disc test is reliable only for *Haemophilus*, *Neisseria*, *Staphylococcus* and *Moraxella catarrhalis*. Exposure times should be at least 10-15 minutes before calling a result negative. The paper disc test utilising a chromogenic cephalosporin as the substrate and indicator can be used for the same organisms and also for certain anaerobes and for *Enterococcus*. These are organisms producing group IIa β-lactamase (plasmid mediated penicillinases inhibited by clavulanic acid). Exposure times are 1 minute for *Haemophilus*, *Neisseria* and *Moraxella catarrhalis*, 30 minutes for anaerobes and 60 minutes for *Staphylococcus* (for greater sensitivity, test growth from zone edge of oxacillin or methicillin disc; weak β-lactamase activity detected in the majority of strains of *Staphylococcus saprophyticus* is of little clinical significance; store discs in freezer but use at room temperature and moisten disc slightly before use) and *Enterococcus*. Testing for β-lactamase activity in other organisms gives misleading information of no clinical significance. *Enterobacter, Serratia, Citrobacter, Acinetobacter, Providencia, Proteus vulgaris* and *Morganella* produce chromosomally determined group I β-lactamases under the control of one or more regulatory genes which initiate production of the enzyme on exposure to the antimicrobial (ie, induction). These regulatory genes have a high rate of spontaneous mutation (1 in every 10^5-10^6 organisms). Because most susceptibility tests use inocula of 10^4 organisms, resistance may not be apparent on in vitro testing. This group can spontaneously mutate to become high level β-lactamase producers (hyperproduction of β-lactamase can occur at levels hundreds of times greater than normal). This renders them resistant to most β-lactam antimicrobials (except imipenem). If these organisms are treated with β-lactam antimicrobials, there is a high risk of selecting out the β-lactamase-producing organisms, which then persist, resulting in treatment failure. For this reason, organisms in this group should be reported resistant to all β-lactam antimicrobials (all penicillins, all cephalosporins, all cephamycins, aztreonam) except imipenem, regardless of susceptibility test results. *Pseudomonas aeruginosa* can also produce inducible β-lactamase, but the frequency of mutation is much lower (1 in 10^9). Therefore, agents such as piperacillin and ticarcillin are still therapeutically useful if they appear susceptible in vitro. Enterobacteriaceae may also produce group IIb β-lactamase (cephalosporinases, including extended broad spectrum β-lactamases active against third generation cephalosporins and monobactams. These are plasmid mediated (mainly involving plasmids of the TEM and SHV series) and are characteristically susceptible to inhibition by clavulanic acid. They have almost invariably been found in *Klebsiella pneumoniae* isolates, though rare instances have been reported in *Escherichia coli*, *Salmonella*, *Citrobacter freundii* and *Enterobacter*. *Klebsiella* isolates from blood cultures or serious hospital infections (eg., ICU/CCU patients), multi-resistant Enterobacteriaceae (ie., resistant or only moderately susceptible to third generation cephalosporins or aztreonam or resistant to aminoglycosides), isolates of Enterobacteriaceae from patients who have been treated with third generation cephalosporins or aztreonam, and Enterobacteriaceae which show resistant colonies within the zones of inhibition of cefotaxime, ceftazidime or aztreonam should be tested for production of extended broad spectrum β-lactamase by Cassal's test. If positive, the isolate should be regarded as resistant to all cephalosporins and penicillins except amoxycillin-clavulanate and ticarcillin-clavulanate. The Vitek ESBL card detects 96% of these strains, but the E test only 65%.

Note that antibiotic susceptibility may be useful as an aid to, or check on, identification. For instance, *Pasteurella* and *Kingella* are always susceptible to penicillin. An oxidase negative and/or large-celled Gram negative bacillus which appears penicillin susceptible should be viewed with suspicion unless it has been identified as belonging to a species which includes penicillin susceptible strains. It should be verified that it is in fact Gram negative (by repeat Gram stain and/or string test and/or vancomycin susceptibility). If this is indeed so, oxidase test and penicillin susceptibility test should be repeated. Likewise, a tetracycline susceptible *Proteus mirabilis* demands checking of identification, susceptibility or both, as does an ampicillin susceptible *Morganella morganii*. Similar considerations apply to nalidixic acid, polymyxin or colistin susceptible Gram positive organisms or resistant Gram negatives. Again, enterococci producing zones $\geq$ 30 mm for ampicillin or $\geq$ 28 mm for penicillin are quite unusual and the speciation should be reexamined. Other resistances which should be checked include ampicillin resistant *Enterococcus*, penicillin resistant *Neisseria meningitidis*, rifampicin or chloramphenicol resistant *Haemophilus influenzae*, penicillin resistant *Streptococcus pyogenes*, penicillin or chloramphenicol resistant *Streptococcus pneumoniae*, vancomycin resistant *Staphylococcus*.

In the case of mixed infections, every effort should be made to find antibiotics to which all significant isolates are susceptible in common.

Baker et al's indicator broth kit is rapid, simple and inexpensive, gives 80-100% agreement with Kirby-Bauer and may be useful, especially for small laboratories and 'field' conditions.

Acquired resistance by chromosomal mutation differs from plasmid mediated resistance in that it forms a single resistance determinant in a single strain. Plasmids may code for multiple antibiotics and may be transferred by conjugation

from one bacterium to another. Under some circumstances, bacteria may be 'cured' of plasmids and lose their resistance. On the other hand, a loss mutation reversing chromosomally acquired resistance is relatively rare. Resistance by either mechanism is not induced by presence of the agent; rather a resistant population is selected by death of sensitive strains. Since acquired chromosomal resistance involves only a single agent (at a time), use of multiple antimicrobials may prevent the emergence of resistant strains. This is less likely to be true with strains showing plasmid mediated resistance since a single plasmid frequently codes resistance to several antimicrobials.

Bacterial tolerance is failure of an antimicrobial to kill the organism, not just inhibit growth. It is due to inhibition or depletion of the autolytic enzyme system within the cell. Tolerance to penicillin has been proposed as one possible explanation for the failure of response of some streptococcal infections to penicillin therapy. This is particularly important in endocarditis, where a bactericidal effect appears essential to cure. Addition of an aminoglycoside usually produces a synergistic effect and reduces the **MBC** to a value close to the **MIC**. Tolerance has also been observed in staphylococci. Penicillin tolerance is usually reflected in vitro by a significant discrepancy between the **MIC** and the **MBC**. The ratio of **MBC** to **MIC** selected for the definition of tolerance has varied from study to study but a value of $\geq$ 32:1 is most commonly used.

Isolates of *Streptococcus pneumoniae* with **MIC**s in the range of 0.1-1.0 mg/L should be reported as being of intermediate or reduced sensitivity or as being moderately resistant to penicillin. Estimates of the prevalence of pneumococci in this group have ranged from zero to 35%. Individuals with pneumonia caused by these organisms may respond to conventional therapy with penicillin, whereas individuals with meningitis have responded irregularly, perhaps because of the inconsistent penetration of penicillin into inflamed meninges.

SUGGESTED MINIMUM QUALITY CONTROL PROCEDURES

- checking inoculum preparation
- checking new batches of media
- weekly outcome testing with control strains of *Staphylococcus aureus, Staphylococcus aureus* (methicillin heteroresistant), *Escherichia coli, Escherichia coli* (ampicillin resistant), *Pseudomonas aeruginosa*, *Haemophilus influenzae*
- participation in an outside quality assurance program
- any reasonable procedures recommended by equipment manufacturers not included in the above
- 'eternal vigilance' for unusual results

Non-cultural Methods

Agglutination Titre: Antibody to antigen on surface of microorganism causes a visible precipitation of microorganism. Useful diagnostic alternative when direct demonstration unsuccessful or not possible. A 4-fold rise in titre between acute and convalescent sera is convincing evidence of recent infection (less may be due to inherent variation of test). A high titre in a single specimen may be significant.

Anti-deoxyribonuclease B: Detects streptococcal infection. Levels of antibody are measured by visualising hydrolysis of DNA, which is linked to a colour reaction. It is consistently elevated with both rheumatic fever and glomerulonephritis, rises later than anti-streptolysin O titre, peaks at 4-6 w and remains elevated longer than anti-streptolysin O titre. The magnitude of response may be suppressed by antimicrobial therapy. Detergents, heavy metals, azide and other chemicals interfere with enzyme and colour reaction.

Anti-streptolysin O Test: Antibody from patient's serum inhibits streptolysin O produced by *Streptococcus pyogenes* (lyses human erythrocytes). Normal in $\approx$ 20% of early rheumatic fever and 50% of glomerulonephritis (especially following skin infection). Peaks at 2-4 w. False positives due to activity of other substances neutralising haemolytic properties of streptolysin O (eg, serum β-lipoproteins in liver disease and bacterial growth in serum).

Complement Fixation Tests: Complement depleted ('fixed') by combination with complex of microbial antigen and antibody. Rise within 2 w of onset, rarely remain raised longer than a few months.

Complement Lysis: Antibody to microbial surface antigen + complement lyses bacterium or enveloped virus. Used in research.

Counterimmunoelectrophoresis: Detection time 30 minutes. Requires special equipment. Availability of quality sera is limited.

C-reactive Protein: Direct latex agglutination test positive in variety of inflammatory and necrotic processes.

Direct Immunofluorescence: Fluorescein-labelled antibody to antigen on microorganism or antigen formed in infected cell seen on microrganism or in infected cell by UV microscopy.

Dye Test: Detects *Toxoplasma gondii.* Usually reliable, though status of disease activity may be uncertain.

Enzyme-Linked Immunosorbent Assay (ELISA, EIA): antibody linked to enzyme reacts with microbial antigen. Specific binding revealed when enzyme causes colour change in substrate. Detection time 4 h. Requires special equipment. Very specific. Requires small sample. Long incubation. Time consuming procedure. Used for *Giardia*, *simplexvirus* virus, many other organisms.

Gel Diffusion: Antibody reacts with diffusible microbial antigen to form precipitation line in gel. Elek test is immunodiffusion test used to identify toxigenic strains of *Corynebacterium diphtheriae* and *Corynebacterium ulcerans.*

Hemagglutination Inhibition Antibody Technique: Inhibition of erythrocyte agglutination by hemagglutinin forming part of surface of virus particle.

Immobilisation Test: Inhibition of motility by reaction with antigen on locomotor organ (flagellum, cilium).

Immune Electron Microscopy: Virus particles clumped by reaction with antigen on surface of virus viewed by electron microscopy. Used in research.

Latex Agglutination: Antibody to microbial antigen adsorbed to latex particles agglutinates latex particles. Detection time < 5 minutes. May require treating specimen to eliminate nonspecific agglutination. Used for *Cryptococcus* and many others.

Mini Vidas: enzyme-linked fluorescent immunoassay performed in an automated instrument; provides assays for *human immunodeficiency virus* p24 antibody, *human immunodeficiency virus* anti-p24 antibody, hepatitis B core antigen IgM antibody, anti-hepatitis B surface antibody, hepatitis B surface antigen, hepatitis A IgM antibody, anti-hepatitis B core antigen antibody, *human cytomegalovirus* IgG antibody, *human immunodeficiency virus* 1+2, *mumps virus* IgG antibody, *measles virus* IgG antibody, *human rubella virus* IgG antibody, *Toxoplasma gondii* IgG antibody, *Toxoplasma gondii* IgM antibody, *human herpesvirus 3* IgG antibody, *Toxoplasma* competition assay, Lyme disease screen, *human cytomegalovirus* IgM antibody, *human rubella virus* IgM antibody, *human rubella virus* IgG antibody, *Chlamydia, Clostridium difficile* toxin A, *simplexvirus*, *respiratory syncytial virus*, *Campylobacter, Escherichia coli* O157, *Listeria, Salmonella* and *Staphylococcus* enterotoxin.

Neutralisation Antibody Titre: Antibody reacting with viral surface antigen necessary for multiplication in experimental animal or cell culture inhibits multiplication and prevents pathological lesions, death or cell damage.

Neutralisation Test: Biological effect of bacterial toxin inhibited.

Nucleic Acid Probes: Useful in detecting *Mycoplasma pneumoniae*, *simplexvirus* and others.

Passive Hemagglutination: Antibody to microbial antigen absorbed to surface of erythrocyte agglutinates erythrocytes.

POLYMERASE CHAIN REACTION: Method of choice in detecting *Chlamydia*. Also useful for *Mycobacterium tuberculosis, M.avium, M.intracellulare,* hepatitis C virus, hepatitis B virus, gonorrhoea, *human immunodeficiency virus*, enterovirus, *Mycoplasma, human herpesvirus 6, 7* and *8*, *human parvovirus B19*, *Bartonella henselae, Plasmodium,* enterohaemorrhagic *Escherichia coli* O111/O157, *Salmonella, Legionella, Entamoeba histolytica, Ross River virus*, *dengue virus 1, 2, 3* and *4*, *Murray Valley encephalitis virus*, *Japanese encephalitis virus*, flaviviruses, *Leptospira*

WHITE CELL COUNT: leucocytosis ($\geq$ 15,000/mm^3) in hospital patients: 47% pneumonia, 38% physiological stress, 29% urinary tract infection, 16% soft tissue infection, 16% *Clostridium difficile* infection, 11% medications or drugs, 6% hematological disease, 6% necrosis or inflammation

Chapter 30

Reporting Results

Significance of Isolates

Diagnostic microbiology laboratories attempt to provide data which allow clinicians to diagnose and manage infectious diseases. In order to achieve this, criteria of pathogenicity must be identified for particular organisms and when laboratory reports are issued these criteria must be applied to the particular patient circumstance.

Misleading information concerning pathogenicity may be conveyed because the relationship of particular isolates to disease is not clearly established and because the information conveyed from laboratory to clinician does not always indicate to the clinician the criteria of pathogenicity upon which the report was made.

Much bad medicine is perpetrated because of poor communication between clinician and laboratory. Firstly, the clinician must make available all relevant information to the laboratory. The clinician who sends a specimen to the laboratory requesting 'swab culture' and omitting any other information can scarcely expect useful bacteriology to be performed. It is manifestly impossible to subject every specimen submitted to every possible investigation or to completely speciate and determine antimicrobial susceptibilities of every isolate. It is also completely impossible to devise a routine which will not regularly permit inappropriate procedures to be performed and appropriate ones omitted unless each specimen is capable of being treated in full knowledge of the individual circumstances.

Errors regularly committed by laboratories (other than technical errors) are most commonly of four kinds: those due to lack of knowledge of what to look for when (eg., neglecting to look for acid-fast bacteria in a specimen from an infected breast prosthesis or discarding a *Streptococcus milleri* isolate from an abscess as a probable skin contaminant *Streptococcus viridans*); a too rigid, blind adherence to an established routine without taking sufficient note of individual circumstances (this includes neglecting the abnormal host and his special predilections for infections that may not occur in the normal individual, and ignoring the type and quality of the specimen); reporting virtually anything that grows and leaving it up to the clinician to decide on the significance (all too often the clinician is apt to think the laboratory must have reported an isolate because it was thought significant and treat it accordingly); and disregarding virtually all isolates except those established through long practice as important in disease. These categories do, of course, overlap. Basically, they are mainly due to ignorance, which hopefully this book will help to dispel. Sometimes they are also compounded by considerations of convenience or commercial interests.

It is necessary to distinguish clearly the circumstances under which an organism may be isolated from a specimen. Firstly, it may be a contaminant, ie, not actually present at the sampled site. This may be because of the intrinsic nature of the specimen or a completely extraneous event. Many specimens are by their nature easily contaminated by bacteria present at intervening (eg, sputum, blood cultures) or adjacent (eg, urines in females) sites. Good technique will minimise many of these but they can never be totally eliminated. Intelligent microscopic examination of specimens will identify most of these instances of contamination (and also many instances of extraneous contamination during collection or transport). An obviously contaminated specimen should just not be processed, since any information it provides will be completely misleading. Extraneous contamination within the laboratory can be largely eliminated by good quality control but will always occur from time to time even in the best laboratory. The microbiologist rather quickly learns to recognise the odd colony off the streak that is obviously an aerial contaminant, the plate contaminant that has been picked up and carried on the streak, and the odd organism that is suddenly appearing in cultures from a number of different specimens on a particular type of medium (or in a batch of stains).

It is, however, all too easy to dismiss the odd colony of a significant organism as a contaminant. In most cases of specimens with a normal flora, this may not be of grave importance, though by no means in all. However, in specimens taken from a normally sterile site, it may be extremely important. In most cases, any contamination will (if not completely extraneous) be skin flora; a single colony of, say, *Haemophilus influenzae* or *Streptococcus milleri* can never be dismissed as a contaminant under these circumstances. It needs to be remembered that organisms are frequently present in very small numbers in such specimens. This means also that they may not be seen in a Gram stain; with a density of 100 organisms/mL (which may often be the case in

meningitis), the chances of seeing the organism in a Gram stain are fairly low. On the other hand, if an organism is seen in a Gram stain in such a specimen, it is extremely unlikely to represent contamination.

Another possibility is that the organism is a transient, one that is adventitiously present at the site but is not capable of establishing itself at the site. The individual circumstances will suggest this possibility, a possibility that can best be established by repetitive cultures from the site.

With respect to microorganisms which are actually established at a particular site, it is important to distinguish between three possible conditions: colonisation, infection and disease. It is possible for a microorganism to colonise a biological site without directly affecting the activities of the host in any manner. This is the case with commensals, which make up the bulk of 'normal flora'. Although cases of true symbiosis between man and his resident flora are rare, such commensals frequently perform the very useful function of helping to prevent infection by more deleterious microorganisms. Commensals normally colonise only non-viable (usually terminally differentiated) cells.

An infection may be said to occur when a parasite is modifying the activities of the host in some way, though not necessarily in such a way, or to such an extent, as to cause disease. This usually implies a degree of invasion of viable cells and a greater turnover of involved host cells.

When the activities of a parasite are such that significant damage to host tissue is caused, disease ensues. This may be a direct effect of the parasite, an effect on some other element(s) of the flora which then produce deleterious effects, or mediated by the defence mechanisms of the host.

Which one of these conditions actually occurs depends on the invasive capabilities of the microbe versus the ability of the host to limit such invasion, and the nature and extent of adverse activities produced by the microbe versus the capacity of the host to nullify such activities or repair their effects.

How does all this translate into practice in the laboratory? I do not propose to give a short list of what to report when for all the different kinds of specimens, since it is impossible to include all the possibilities in such a list. The following guidelines should, however, provide at least some of the answers. Instances of obvious extraneous contamination are excluded in these guidelines.

All isolates from blood cultures should be speciated and their biograms and antibiograms recorded. All isolates of Gram negative bacteria and of fungi should be reported, as should all isolates of Gram positive bacteria except single isolates of coagulase negative staphylococci, *Bacillus, Corynebacterium* and *Propionibacterium acnes*. In any case, multiple isolates of the same species with the same biogram and antibiogram should be reported.

In the case of specimens from other normally sterile sites, any growth should be reported.

In specimens from sites with a normal flora, only organisms implicated as regularly causing disease at the particular site in the particular patient population represented by the individual should be reported. If it is not possible to obtain information about the patient, organisms potentially significant under certain circumstances should be reported together with an indication of these circumstances. There is a necessary proviso to this: unless there is clear evidence suggestive of an infection caused by this organism. This proviso is necessary because there must obviously occur cases of significant infection due to an organism not previously reported, or only rarely reported, as causing such infections. Our knowledge is not, and never will be, complete on such matters.

What constitutes clear evidence of an infection involving the organism (in a particular case)? Some years ago, the author proposed the following set of postulates of pathogenicity to be used both in the many cases where Koch's postulates are not applicable and in the instance of such 'private pathogens'. The organism must: (1) either be shown to be producing infection at the biological site in question or produce infection in a specific cell system replicating the conditions prevailing at the relevant site; and (2) either be shown to be producing effects which constitute, or can be quantitatively correlated with, the symptoms of the condition, or be shown to be capable, under the conditions prevailing at the site, of producing such effects; (3) evidence of a quantitative relationship between such effects and the activity of the organism must be obtained; (4) it must be demonstrated further that the organism is inhibited in its capacity for producing these effects by agents mitigating the symptoms of the condition; (5) presumed cause and effect through the sequence of events leading to the disease state must be shown to be temporally related.

All this, of course, is a little involved and, despite many years work, is not completely capable of realisation and especially not as a routine laboratory test.

At the present time, evidence of an infection involving a particular organism is usually best established by careful microscopic examination of the specimen. Evidence of infection may be provided by presence of excess numbers of leucocytes, especially non-viable leucocytes. This does not, of course, definitively establish that the

suspect organism is responsible for the process, even if it is the only organism present, but it does at least establish an index of suspicion.

If a bacterium is intracellular, it is a pathogen. It may, however, be necessary to establish unequivocally that the organism is in fact intracellular. This can be done for phagocytes by using fluorescence and extracellular quenching, as in the method of Goldner et al, and for tissue by the use of Sowter and McGee's Gram stain.

It is important to realise that organisms which are normal flora at a site may yet be significant under certain conditions. For example, *Streptococcus agalactiae* is normal flora in the female genital tract. However, it can cause problems in post-operative patients and in patients with IUDs. It is also of importance in pregnant women, since it may be transmitted to the baby during birth and cause a potentially fatal infection. Again, *Staphylococcus aureus* is frequently present in low numbers in the female genital tract without causing problems but can be significant in post-operative and postpartum patients. It also represents a potential cause of toxic shock syndrome in females using tampons. Thus, there is some necessity for reporting both these organisms, but the conditions under which they may be significant should be indicated in the report.

URINE CULTURES: Relevant considerations in interpreting urine cultures include: viable bacterial count; whether culture is pure or mixed; cell type in urine microscopy (leucocytes, epithelial cells); presence or absence of bacterial inhibitors; patient's clinical history. The following general guidelines can be given.

A pure growth of an organism at $> 10^5$ organisms/mL represents probable UTI and the organism should be identified and susceptibility tests performed.

A pure growth of an organism at 10^4-10^5 organisms/mL indicates possible UTI and the organism should be identified and susceptibility tests performed.

The presence of 2 organisms in equal numbers at $> 10^5$ organisms/mL may indicate either UTI or faulty collection. Both organisms should be identified and susceptibility tests carried out on both.

The presence of 2 or 3 organisms at $> 10^5$ organisms/mL, with one organism clearly predominant indicates probable UTI caused by the predominant organism, which should be identified.

A mixture of 3 or more organisms in equal numbers at $\geq 10^5$ organisms/mL, or of 2 or more organisms at 10^4-10^5 organisms/mL should be reported as a mixed growth with no species predominating.

A pure growth of an organism at 10^3-10^4 organisms/mL from a symptomatic female or a male with prostatitis or from any patient with leucocytes $\geq 100/\mu L$ represents possible UTI and the organism should be identified and susceptibility tests preformed.

A pure growth of an organism at 10^3-10^4 in an asymptomatic patient, or in the absence of leucocytes, and with bacterial inhibitors absent indicates no UTI and should be reported as no significant growth.

A pure growth of an organism at $\geq 10^3$ in the presence of a bacterial inhibitor may indicate treatment failure. Refer to any previous results, identify the organism and perform susceptibility tests.

All isolated organisms from a suprapubic collection, ureteric or in-out catheter (not indwelling catheter) should be identified and reported with susceptibilities and the colony count to the nearest hundred.

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